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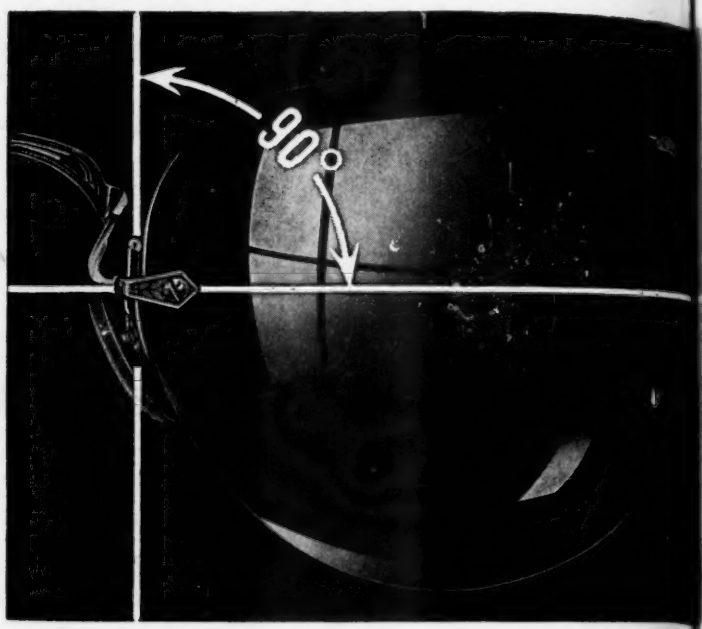

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AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 30 NOVEMBER, 1947 NUMBER 11

VITREOUS INFECTIONS AND STREPTOMYCIN*

EXPERIMENTAL STUDIES

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Vitreous infections are fortunately not frequent. Nevertheless, they do occur and are extremely difficult to treat. They may occur as a result of bacteria spreading from other parts of the body or eye, following penetrating or perforating injuries, and after intraocular surgery. With the advent of the sulfonamides and penicillin impetus was given to experimental studies concerning vitreous infections.[1-3]

There are certain principles that must be followed in treating vitreous infections with an antibacterial drug. In order for any chemotherapeutic agent to be effective it must be able to reach the infected tissue in adequate concentration. The organism responsible for the infection must be susceptible to the chemotherapeutic agent. When the therapeutic drug is present in the infected tissue in adequate concentration, it should not produce damage to the tissue.

Systemically administered sulfonamides will reach the vitreous humor in high concentrations[4-7] and in such concentrations will not damage the vitreous body. However, when tried in a standard experimental infection, systemically administered sulfonamide therapy usually failed.[2,8,9] Direct intravitreal injections of sulfonamides as employed by von Sallmann and coworkers[1] were not successful in controlling experimental vitreous infections. There are, however, a few reports of direct intravitreal injections of sulfonamides controlling infection in human eyes.[10] Direct intravitreal injections of sulfonamides produce vitreous, retinal, and choroidal damage.[8,11]

Penicillin has been shown to penetrate poorly from the blood stream into the vitreous humor[3,12-16] of the normal and inflamed eye. Corneal baths, corneal iontophoresis, subconjunctival and anterior-chamber injections produced higher intravitreal concentrations of penicillin than did the systemic route.[3,12,13] However, although these local measures and massive systemic doses had some success in controlling experimental vitreous infections, not one was as effective as direct intravitreal injections of penicillin.[1-3,16,26]

Direct intravitreal injections of penicillin occasionally produced vitreous opacities, retinal and choroidal degeneration around the sites of injections. Some eyes, so injected, showed only temporary alterations of structure similar to those following normal saline injections. Clinical cases are beginning to appear in the literature in which vitreous infections have been successfully treated by direct injections without producing untoward dam-

* Presented before the Section of Ophthalmology, College of Physicians of Philadelphia, April 24, 1947. From the Department of Ophthalmology, University of Pennsylvania, and Harrison Research Surgery Department, University of Pennsylvania. Streptomycin used in this study was supplied by Merck & Co., Rahway, New Jersey.

age.[17] In some hands, experimental intravitreal penicillin injections have proved quite damaging, but this has been attributed to an impure form of penicillin.[18] Five thousand units of purified penicillin in 0.1 cc. of water have been placed in the vitreous with little subsequent reaction and no ophthalmoscopically visible changes.[26] Because of the possibility of damaging the intraocular structures of the posterior segment with commercially available penicillin, ophthalmologists hesitate to use such therapy. Less damaging procedures are usually tried first and intravitreal injection used only as a final hope.

TABLE 1

VITREAL CONCENTRATIONS OF STREPTOMYCIN FOLLOWING SUBCONJUNCTIVAL, ANTERIOR-CHAMBER AND DIRECT INTRAVITREAL INJECTIONS

Micrograms per cc. of Vitreous Humor		
Time after injection	30 Min.	120 Min.
	Subconjunctival Injection	
Rabbit	O.D.	O.S.
1	3 μg./cc.	3 μg./cc.
2	1 μg./cc.	3 μg./cc.
3	trace	5 μg./cc.
	Anterior-Chamber Injection	
	O.D.	O.S.
4	trace	20 μg./cc.
5	15 μg./cc.	25 μg./cc.
6	10 μg./cc.	15 μg./cc.
	Vitreal Injection	
	O.D.	O.S.
7	70+ μg./cc.	70+ μg./cc.
8	70+ μg./cc.	70+ μg./cc.
9	70+ μg./cc.	70+ μg./cc.

Because it has been shown that streptomycin penetrates poorly from the blood stream into the normal vitreous humor,[19] it is likely that local administration of streptomycin will have to be used in therapy of vitreous infections. Studies of vitreous-humor concentrations following local methods of administration of streptomycin have not as yet been reported, and are included in this present paper.

Experimental Studies

Part 1

Streptomycin was administered subconjunctivally. It was also injected directly into the anterior chamber and directly into the vitreous humor. Blue-eyed chinchilla rabbits weighing between 3 to 4 kilos were used. Six normal eyes were used for each type of injection. Subconjunctival injections were made with 100,000 micrograms/0.2 cc. of normal saline and vitreous injections with 100,000 μg./0.1 cc.

Direct anterior-chamber injections were made with 100,000 μg./0.1 cc. The anterior chamber was punctured and approximately 0.1 cc. of aqueous humor was drawn into the syringe containing 100,000 μg. in 0.1 cc. and approximately 0.1 cc. of the syringe mixture was reinjected into the anterior chamber. In this way approximately 50,000 μg. were placed into the anterior chamber.

Vitreous humor specimens for each type of administration were withdrawn at 30 minutes after injection in three eyes and after two hours in three eyes. Specimens were analyzed by the method described by Stebbins and Robinson[20] using their strain of staphylococcus aureus.

The results of these studies are recorded in Table 1. It is evident that anterior-chamber injections produce higher concentrations than the subconjunctival route[8] in the vitreous humor of the normal eye. This had been shown previously to occur with penicillin.[3] All these methods of local administration of streptomycin produced higher intraocular concentrations than those reported for the usual systemic doses.[19]

Subconjunctival injection was always followed by marked local injection and chemosis that largely subsided in 8 to 12 hours. Anterior-chamber injection produced conjunctival edema, pericorneal in-

jection, and signs of iritis. Most of these changes disappeared in 36 to 48 hours. In one rabbit, lenticular opacities developed. Because of these lens changes the anterior chambers of six additional eyes were injected with concentrations of streptomycin ranging from 5,000 to 100,000 units per injection. Care was taken not to inject the material with excess force and to be certain that the needle did not touch the lens. In none of these did any permanent lens changes develop.

Posterior-segment injections were made with concentrations ranging from 40 to 100,000 μg. in 0.1 cc. into 12 rabbit eyes. The results are listed in Table 2. All produced clouding of the vitreous humor. The globe became red and vitreous opacities developed. Slight clouding of the cornea occurred temporarily for a few hours after each injection and was probably due to a temporary increase in intraocular pressure. After two days large white areas could be seen in the retina around the site of injection in all six eyes that received 5,000 to 100,000 units per injection. These were areas of retinal and choroidal exudation which gradually changed to patches of degenerated tissues. These patches were localized to the side of the original site of injection except in the eye that received 100,000 units. Here the entire posterior segment was involved, preventing a view of the fundus.

It is thus apparent that intravitreal injections of streptomycin produced damage similar to that seen with penicillin. However, it is noteworthy that concentrations below 800 μg. of streptomycin can be injected with very little subsequent reaction similar to that seen following the injection of normal saline alone.

Anterior-chamber injection of streptomycin produced no permanent damage and did provide levels that might prove helpful in controlling vitreous infections. Anterior-chamber injections of penicillin

TABLE 2

RESULTS OF POSTERIOR-SEGMENT INJECTIONS OF VARIOUS CONCENTRATIONS

Rabbit No.	Micrograms of Streptomycin per Injection	Ocular Reaction
1	100,000	Exudation and later organization of posterior segment No fundus view
2	50,000	Exudation and later degeneration of retina and choroid on side of injection
3	20,000	Exudation and later degeneration of retina and choroid on side of injection
4	10,000	Exudation and later degeneration of retina and choroid on side of injection
5	10,000	Exudation and later degeneration of retina and choroid on side of injection
6	5,000	Exudation and later degeneration of retina and choroid in quadrant of injection
7	3,000	Exudation and later degeneration of retina and choroid in quadrant of injection
8	1,500	Exudation and later degeneration localized about site of injection
9	800	No reaction except immediately at site of injection
10	400	No reaction except immediately at site of injection.
11	200	Slight exudation in addition to damage at site of injection
12	40	No reaction except for damage at site of injection

were not as successful in controlling experimental vitreal infections as the direct intravitreal injection technique.[3] One hesitates to disturb the integrity of an eye by any sort of intraocular injection unless he is certain that the diagnosis is correct, that the infection will respond, and that matters will not be made worse by such therapy. Corneal iontophoresis and subconjunctival injection can give high concentrations in the anterior chamber but not as high as those reached by direct anterior-chamber injection. It apparently requires very high anterior-chamber concentrations of drugs such as streptomycin and penicillin in order for them to pass posteriorly through the iris-lens barrier. In an effort to find another method by

which these antibiotics could reach the vitreous without direct intraocular injection, further studies with iontophoresis were undertaken.

TABLE 3

CONCENTRATION OF PENICILLIN IN VITREOUS HUMOR FOLLOWING RETROBULAR INJECTIONS AND RETROBULBAR INJECTIONS PLUS IONTOPHORESIS

Units per cc.			
Retrobulbar Alone		Retrobulbar plus Iontophoresis	
30 Min.	*120 Min.*	*30 Min.*	*120 Min.*
0	0	.3	.3
0	0	.3	.3
0	0	.5	.3
0	0	.3	.4

It is known that ions do not pass through circulating fluid and it is assumed that they are carried away by such fluid. This explanation has been applied to the vascular sponge of the choroid. It had been accepted generally that ions could not be introduced into the posterior segment of the eye through the choroid.[21, 22] However, this hypothesis has been disproved recently by von Sallmann.[23, 24] He reported driving anions through the sclera, choroid, and retina into the vitreous. For these reasons studies were run to determine the ability of penicillin and streptomycin to penetrate the posterior segment of the eye when aided by iontophoresis.

PART 2

Instead of applying electrodes directly to the sclera, the antibiotics were injected retrobulbarly and a glass electrode was applied over the corneal surface. The corneal electrode was filled with normal saline and the positive pole attached to it. The negative electrode was placed behind the neck. These poles were reversed for streptomycin. A current of 3 to 5 milliamperes was applied for five minutes and the vitreous humor specimens withdrawn for analysis at 30 minutes and two hours. Penicillin analyses were done by the technique described by Rammelkamp,[25] and streptomycin according to the Stebbins and Robinson[20] method. Fifty-five thousand units of penicillin in 2 cc. of saline were injected retrobulbarly and 200,000 units of streptomycin in 2 cc. of saline. The results are recorded in Tables 3 and 4.

It is evident that retrobulbar injection

TABLE 4

CONCENTRATION OF STREPTOMYCIN IN VITREOUS HUMOR FOLLOWING RETROBULBAR INJECTIONS AND RETROBULBAR INJECTIONS PLUS IONTOPHORESIS

Micrograms per cc.			
Retrobulbar Alone		Retrobulbar plus Iontophoresis	
30 Min.	*120 Min.*	*30 Min.*	*120 Min.*
0	0	trace	12
0	trace	12	15
0	0	15	13
0	0	13	15

plus iontophoresis did aid the penetration of each antibiotic into the vitreous humor.

The levels for streptomycin are approximately the same as those following anterior-chamber injection (see table 1). Vitreous concentrations of penicillin were likewise similar to those reached by anterior-chamber injections according to an earlier report.[3] Following retrobulbar injections considerable chemosis and injection of the globe occurred. This reaction subsided within 8 to 12 hours. Iontophoresis of the duration and strength used produced slight, temporary clouding of 5 of 16 corneas but no permanent change.

PART 3

To determine the relative efficiency of these methods against vitreal infection the following studies were undertaken: 0.1 cc. of a diluted 18-hour broth culture of B. coli (100,000 organisms per cc. in-

TABLE 5

VITREOUS INFECTIONS DUE TO 1,000,000 BACTERIA-COLI ORGANISMS AS INFLUENCED BY VARIOUS FORMS OF LOCAL STREPTOMYCIN THERAPY

Type of Therapy	No. of Eyes	No. of Eyes Degenerated in 3 weeks	No. of Eyes Degenerated in 4 months
1. No Therapy	6	6	
2. Intravitreal Injection	6	0	6
3. Anterior-Chamber Injection	6	2	4
4. Retrobulbar Injection	6	6	
5. Retrobulbar Injection plus Iontophoresis	6	0	6

hibited by 3 μg. of streptomycin per cc.) was injected into the vitreous humor of 30 eyes. There were approximately 1,000,000 organisms in each injection. Within 30 minutes after injection of the organisms, 100,000 μg. of streptomycin in 0.1 cc. were injected into the vitreous of six eyes. Six eyes received 100,000 μg. of streptomycin in the anterior chamber. Twelve eyes were injected retrobulbarly with 200,000 units of streptomycin in 2 cc. of saline. Six of the eyes with retrobulbar injections of streptomycin were treated also with iontophoresis. The negative pole was placed on the corneal glass electrode as in the experimental studies mentioned above. The same current and time for iontophoresis were used as in the preceding experiment. Six eyes had only injections of the organism and no streptomycin therapy. All eyes received daily atropine drops to facilitate ophthalmologic examination.

These studies were then repeated using 20,000 organisms per injection. (table 6). Six eyes were used for each type of therapy and six received no streptomycin.

The untreated eyes receiving 1,000,000 organisms showed marked vitreous abscesses in 16 hours that extended rapidly into the anterior chamber and caused complete degeneration of the eye within 2 to 3 weeks. The untreated eyes that received approximately 20,000 organisms showed vitreous abscesses that spread to the anterior segment in 5 to 7 days and gradually degenerated to phthisis bulbi in 4 to 5 weeks.

Not one of the treated eyes that received 1,000,000 organisms recovered (see table 5). Those that were injected directly into the vitreous with the streptomycin showed a fairly localized vitreous abscess for the first 5 to 7 days but these gradually extended and the eyes degenerated slowly during the next four months.

The six eyes treated with retrobulbar injections of streptomycin alone were completely degenerated within 2 to 3

TABLE 6

VITREOUS INFECTIONS DUE TO 20,000 BACTERIA-COLI ORGANISMS AS INFLUENCED BY VARIOUS FORMS OF LOCAL STREPTOMYCIN THERAPY

Type of Therapy	No. of Eyes	No. of Eyes Degenerated in 5 Weeks	No. of Intact Quiet Eyes after 4 months
1. No Therapy	6	6	0
2. Intravitreal Injection	6	0	6
3. Anterior-Chamber Injection	6	0	3
4. Retrobulbar Injection	6	6	0
5. Retrobulbar Injection plus Iontophoresis	6	0	4

weeks. The six eyes treated with retrobulbar streptomycin injections plus iontophoresis showed localized vitreous abscesses for the first week and then gradually degenerated within the next 5 to 6 weeks.

Eyes treated with anterior-chamber injections varied. Three of the eyes required 5 to 6 weeks for degeneration and three degenerated within 2 to 4 weeks.

In the eyes infected with 20,000 organisms, intravitreal injection controlled all six so treated. These all showed vitreous abscesses that did not extend but remained localized and subsequently organized allowing only a partial view of the fundus. The vitreous never completely cleared but after four months the anterior segments were clear and the globe maintained its form and intraocular pressure.

Four of the eyes treated with retrobulbar streptomycin plus iontophoresis showed a partial fundus view, an intact globe, and quiet anterior segment after four months. The other eyes were soft and degenerated by the fourth month. None of the eyes treated with retrobulbar streptomycin alone differed from the control eyes.

Three of the eyes that received streptomycin in the anterior segment were still intact after four months but only a narrow view of the fundus could be obtained. The anterior segment was quiet and the intraocular pressure not lowered. One eye maintained its shape and intraocular pressure and had a clear anterior segment. Aside from a faint red reflex, no fundus details could be seen in this eye. The other eyes degenerated within two months.

These results indicate that intravitreal injection, retrobulbar injection plus iontophoresis, and anterior-chamber injection of streptomycin all lessened the severity of the infectious process. When fewer organisms were used, these forms of therapy were more successful. In this small series, direct intravitreal injections of streptomycin were superior to the other methods. Retrobulbar streptomycin plus iontophoresis was slightly better than direct anterior-chamber injection.

Although these results are not absolute, they do suggest that retrobulbar streptomycin plus iontophoresis may aid in controlling vitreous infections.

The experimental data concerning vitreous infections shows that the best results are obtained when therapy is instituted early[1, 2] before the infection can become firmly established and the vitreous disorganized. In eyes in which there is a doubt concerning the severity of the posterior-segment infection, when one cannot be certain that the vitreous infection will be overwhelming, one may hesitate about using direct intravitreal injection of an antibiotic because of the possible damage from such an injection.

In such eyes some form of local administration of penicillin or streptomycin should be employed. One should not rely solely on massive systemic doses of penicillin or streptomycin.[27] The local routes that may be employed are subconjunctival injection, anterior-chamber injection, and retrobulbar injection plus iontophoresis.

It must be pointed out that these procedures have not been tried in human eyes. Also, not one of these forms of therapy was repeated in the above experiments. It is possible that daily repetition of anterior-chamber or retrobulbar injection plus iontophoresis may have been more effective.

Conclusions

1. Retrobulbar injections of streptomycin and penicillin plus iontophoresis produced vitreous-humor concentrations equal to that reached with direct anterior-chamber injections and superior to those

following subconjunctival injection.

2. Direct intravitreal injection of streptomycin, retrobulbar injection plus iontophoresis, and anterior-chamber injections reduced the severity of experimental vitreous infections due to bacteria coli. They were effective in the order listed.

3. Direct intravitreal injections of streptomycin produced retinochoroidal exudation and subsequent degeneration. In concentrations below 800 μg. per injection, the damage was minimal and limited to the site of injection.

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PIGMENTATION OF THE PALPEBRAL CONJUNCTIVA RESULTING FROM MASCARA*

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Several years ago, during the course of a routine examination of a middle-aged woman, a granular, stippled pigmentation was noted under the palpebral conjunctiva of both upper lids. The nature of the lesion was not known and no clue was obtained as to its cause. After 10 months, the condition showed no appreciable change and a drawing was made (fig. 1). The pigmentation was situated at each extremity of the tarsus on a level with its upper border. It was located under the conjunctiva rather than in the conjunctiva. Over the pigmented area there was a folliculosis and slight congestion. The condition was identical in both lids. After 2½ years, there had been some extension of the pigmentation and another drawing was made (fig. 2). At each extremity of the tarsus, and particularly at the temporal end, the pigmented area had broadened and had extended horizontally so that it could be seen as a narrow line along the upper border of the tarsus, fading out in the central portion. In addition, a mottled, deep-seated, bluish-black pigmentation could be seen rather faintly under the conjunctiva of the lower lid.

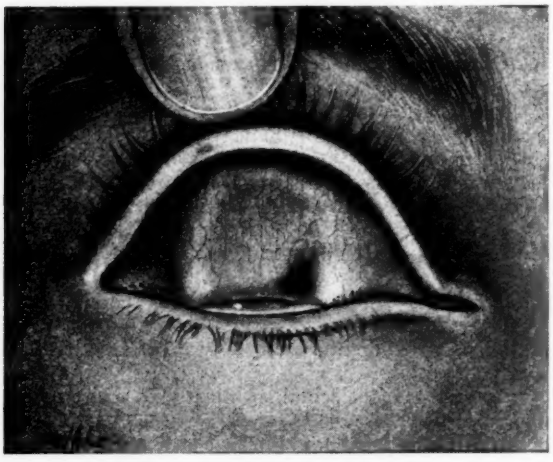

Fig. 1 (Reese). A stippled pigmentation situated at each extremity of the tarsus on a level with its upper border.

During the period this case has been followed, six additional cases have been observed. Except for minor variations they have all been of similar pattern.

* Read at the 82nd annual meeting of the American Ophthalmological Society, San Francisco, California, June, 1946.

The location is always the same, varying only in that some are more pronounced at each extremity of the tarsus (fig. 3), and particularly the temporal extremity, while others manifest themselves mostly along the upper border of the tarsus. The color varies from black to a dirty light brown. The pigment is situated under the conjunctiva and always has a granular appearance. Under higher magnification it can be resolved into irregular punctate dots. There is always an associated folliculosis. The symptoms referable to the condition are mild if any. Symptoms that the patients gave having possible connection with the lesion are: burning, redness, and itching of the eyes, feeling of sleepiness, roughness and swelling of the lids, and desire to blink the eyes excessively. All of the patients were women ranging in age from 31 to 55 years.

Fig. 2 (Reese). The same case as shown in Figure 1 after 2½ years. There is an increase in the pigmentation at each extremity of the tarsus, particularly on the temporal side. The pigmentation has also extended horizontally as a narrow line along the upper border of the tarsus fading out in the central portion. In addition, there is a mottled, deep-seated, bluish-black pigmentation faintly seen under the conjunctiva of the lower lid.

Biopsy material was removed from the most marked case (fig. 3) at a site lateral to the tarsus. The hematoxylin and eosin stain (fig. 4) showed accumulations of black amorphous pigment in follicles and in the stroma under the follicles. The pigment granules were located in or upon stroma cells or were free in the tissue. They were not in macrophages or giant cells and therefore had excited no foreign-body reaction. There was no pigment in the conjunctiva, and no granules could be detected making their way through the epithelium. The follicles were composed of lymphocytes and plasma cells. Bleached sections (fig. 5) showed the pigment unaffected. Sections on which the Turnbull stain was employed showed that the pigment contained no iron.

In an attempt to determine the nature of this lesion, consideration was given to various types of pigmentation of the conjunctiva. Congenital melanosis or acquired precancerous melanosis would not be sym-

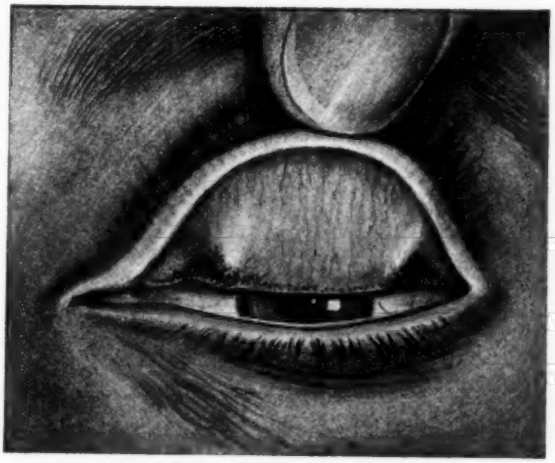

Fig. 3 (Reese). This shows the characteristics of the lesion in the most marked case encountered. The biopsy material was taken from the temporal extremity of the tarsus.

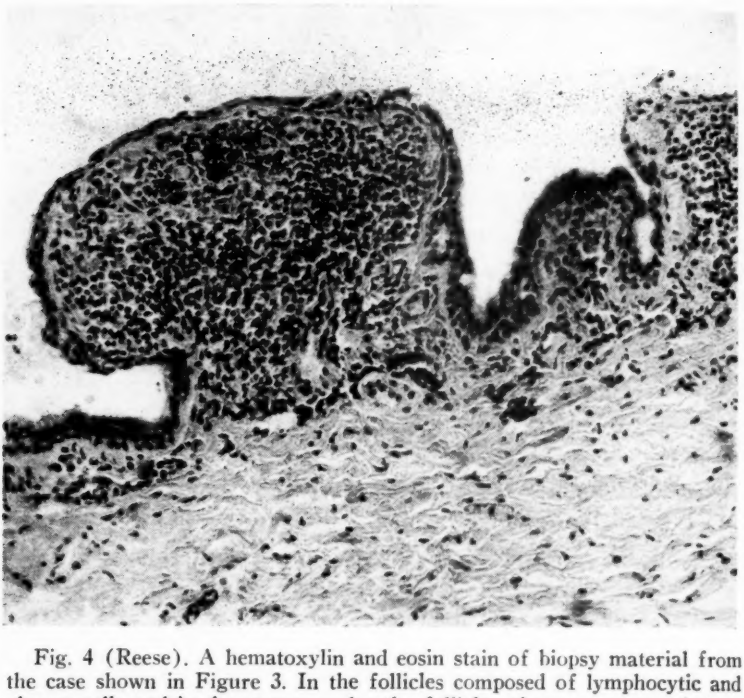

Fig. 4 (Reese). A hematoxylin and eosin stain of biopsy material from the case shown in Figure 3. In the follicles composed of lymphocytic and plasma cells and in the stroma under the follicles, there are accumulations of black-pigment granules in or around stroma cells or free in the tissue.

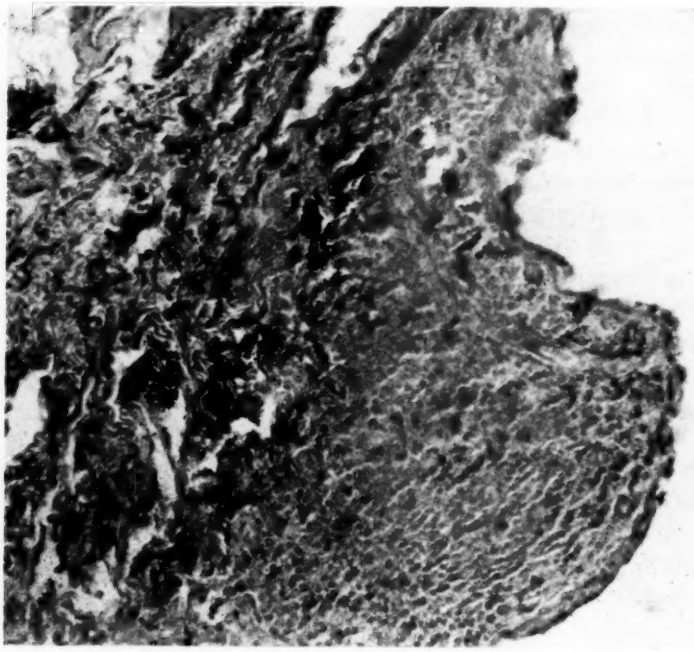

Fig. 5 (Reese). A bleached section of the biopsy material showing the pigment unaffected.

metrical and bilateral and, furthermore, the fact that the pigment is not melanin is indicated by the histologic sections which show, among other things, its failure to bleach. It is not hematogenous pigment because the Turnbull stain showed the absence of iron, and there is no known source of extravasated blood or hemolyzed blood from some systemic condition. Ectogenous or endogenous ochronosis cannot be seriously considered because the location of the pigmentation is not at an exposed site; there is no history of contact with any of the phenol group, no hereditary history, and no alkaptonuria. The condition is not argyrosis because there is no history of local use or ingestion of silver. Furthermore, the location and appearance are not consistent with argyrosis, and the sections rule it out. There is no history to support the occurrence of pigmentation from the long use of adrenalin (I have seen two such cases and they showed jet-black punctate deposits under the palpebral conjunctiva of the lower lid). In the cases reported here, there is no evidence of Addison's disease, no history of exposure to or the use of arsenic, gold, iron, aniline products, indelible substances, or colored inks.

All of the patients were women, five of whom admitted the constant use of mascara and one of whom denied its use so vehemently as to become suspect. One was on the stage and used a great deal of make-up. Off the stage she used, in addition to mascara, eye shadow on the skin of the upper lid. On the stage a process called "beading" was included in her make-up. This consisted of putting a heated black wax on the lashes. She stated that this invariably got in her eyes.

According to the best references I could obtain, mascara is composed of the following:

	Percent
Glyceryl monostearate	10
Triethanolamine	3
Stearic acid	15
Petrolatum	20
Gelatin	2
Water	17
Beeswax	25
Prepared lamp black	8

The appearance and staining reactions of the pigment in the biopsy sections are consistent with its being lamp black. However, there is some evidence that the pigment did not exist as such in the mascara but was precipitated in the tissue. This evidence is the lack of pigment in or adjacent to the epithelium, its location well under the epithelium and sometimes quite deep in the stroma, its close relation to the stroma cells and the tissue interstices, and the absence of a foreign-body type of reaction. If the pigmentation discussed here occurs as the result of precipitation in the tissue, it would be comparable in this respect to the pigmentation from silver which, however, has a predilection for the elastic fibers.

If mascara is the source of the pigmentation, then there must be some individual contributing factor, because everyone who uses mascara does not develop a pigmentation. Only two of the patients considered themselves allergic. The constant presence of follicles is consistent with an allergic reaction but eosinophiles are absent. The use of no one brand of mascara was common to all the patients.

It is concluded that the pigmentation of the palpebral conjunctiva described here results from the use of mascara or allied pigment-bearing cosmetics but that there is some factor peculiar to the individual determining its occurrence.

As women using mascara would, no doubt, consider this pigmentation and its possible attending mild symptoms a cheap price to pay for allure and glamour, the treatment, which is to stop the use of mascara, is probably of no avail

73 East 71st Street (21).

ACUTE REVERSIBLE CATARACT IN CHICKEN DUE TO VARIOUS NITROCOMPOUNDS*

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Since the early clinical reports 12 years ago by Horner, Boardman, Cogan, and others on cataracts after prolonged intake of dinitrophenol, an extensive clinical literature on this cataract has accumulated. Horner reviewed this literature in 1942.[1] An identical type of cataract was described due to intake of dinitrocresol which had been used in Scandinavia for weight reduction.[2]

According to Horner, only 0.86 percent of all individuals who have ingested dinitrophenol are afflicted with cataract, and no correlation to the amount of drug taken, nor to the duration of time during which it had been taken, nor to the age of the patient could be established. In view of the low incidence, it is of interest that this cataract has been described in successive generations of a family,[3] and that some years ago dinitrophenol cataract was seen in the Wilmer Institute in a pair of identical twins. This suggests that a genetic predisposition plays an important role in the susceptibility to this cataract. This notion is strengthened by the fact that in spite of extensive experiments of long duration by many authors it has been found impossible to produce dinitrophenol cataract experimentally in various other species; namely in rats, rabbits, guinea pigs, and dogs, although Bettman[5] observed D.N.P. cataract in a special strain of mice. In contrast to the unsuccessful experiments in various other species, Robbins was able to produce experimental D.N.P. cataract in baby ducks and baby chicks with close to 100-percent results, although the upper age limit for the susceptibility was rather low.[4] These observations have been essentially confirmed and somewhat extended by Bettman,[5] while Dietrich and Beutner[6] failed to produce cataracts with two mononitrophenols in chicks with Robbins' procedure.

Recently, Petty and Martin[12] observed some slowing of the onset of D.N.P. cataract by thiouracil, but they could not lower the incidence of its occurrence.

In addition to the obvious genetic predisposition, the complexity of the pathogenetic problem is illustrated by the facts (1) that the D.N.P. cataract in birds develops acutely in contrast to the chronic cataract in human beings, and (2) that it is, according to Bettman, and to my own observations, reversible even in spite of the continued intake of the drug. It appeared to be desirable to pursue the experiments on chicks more systematically because the regular susceptibility of this species would promise to provide some foothold on the pathogenesis of this cataract.

The following experiments were designed to standardize the conditions for the experimental production of the D.N.P. cataract, to test related com-

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I am indebted for the supply of some of the compounds used in this study to Dr. L. B. Hellerman, department of biochemistry, Johns Hopkins Medical School; Dr. D. E. Kvalnes, E. I. Du Pont Company, Wilmington, Delaware; and Dr. Guggenheim, Hoffman-LaRoche Company, Basel, Switzerland.

The drawings of Figures 1, 1a, 2, and 2a were made by Mrs. A. S. Burgess.

pounds for their cataract-producing capacity, and to correlate the occurrence of the cataract with other biologic and metabolic effects of these compounds. While the first two of these approaches yielded interesting observations, the latter one—that is, the correlation with other effects of the drug—is so far in a quite fragmentary state.

Robbins produced the cataract by mixing dinitrophenol with the diet fed to the animals. My preliminary experiments with varying concentrations of 2, 4-D.N.P. in the diet showed that the occurrence of cataract was dependent on the amount of D.N.P. ingested over a given period of time, and that the threshold concentration of D.N.P. in the diet of baby chicks was 0.1 percent.

The standard procedure then adopted was the administration of the compound as a 0.2- to 0.4-percent solution in peanut oil (with a few compounds in water) in a single dose by stomach tube or intramuscularly. With this procedure, cataracts developed promptly after 1 to 1½ hours in any number of different strains I have tested. The threshold dose is 20 micrograms (1/50 of a mg.) per gm. bodyweight. Cataracts developed promptly also in adult chickens with this procedure, and the failure to produce cataracts in older animals with the ordinary feeding technique in the diet may be due to the fact that older animals have a relatively smaller food intake, in relation to their bodyweight, than young ones.

The first opacities are seen around the suture lines at the anterior pole of the lens (fig. 1) but, after a few hours, the anterior and posterior cortex become diffusely opaque. The suture lines at the anterior pole often gape in an early stage. Under the dissecting microscope, the lens fibers surrounding the anterior pole have a brittle appearance, and innumerable minute structures with the appearance

Fig. 1 (Buschke). Beginning dinitrophenol cataract in chick, with gaping suture lines at anterior pole.

Fig. 1a (Buschke). Appearance of lens under dissecting microscope in early dinitrophenol cataract of chick.

of tiny vacuoles are seen. I could not decide whether these vacuoles were inside or surrounding the individual lens fibers (fig. 1a). With doses with which the animals survive, the lenses become spontaneously clear again after about 24 hours. With the disappearance of the anterior opacities the posterior opacities become more clearly visible (fig. 2).

In feeding experiments, the lenses become clear again with suitable doses after a few days even in spite of continued presence of the drug in the diet. However, systematic experiments have not as yet been done with repeated chronic application of the drug by injection and, therefore, it cannot be excluded, at present, that the spontaneous recovery in continued feeding experiments may be

Fig. 2 (Buschke). Posterior polar lens opacities seen during recovery period from dinitrophenol poisoning in chicken. (Composite drawing.)

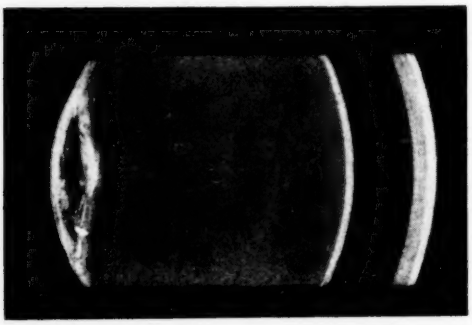


Fig. 2a. (Buschke). Appearance of lens opacities, in the same stage as shown in Figure 2, as seen in the narrow beam of the slitlamp.

due to a diminished food, and thus drug, intake.

Attempts to produce the D.N.P. cataract in vitro had, similar to Bettman, essentially negative results. Whole eyes or removed lenses were kept in varying concentrations of D.N.P.—sodium salt in Tyrode's solution or beef aqueous, or the solutions were injected into the vitreous of the enucleated eye after removal of some intraocular fluid. In none of these experiments were the opacities which developed of the same degree as those in living animals, and, in fact, they were not significantly different from the controls. Eyes were also removed 40 minutes after systemic, in vivo, poisoning of chicks with D.N.P. and stored in a moist chamber at body temperature; some opacities developed in the lenses of the enucleated eyes, but even here they seemed to be less extensive than in vivo. It appears, therefore, that some factor other than or in addition to D.N.P. is required for the development of the cataract, and that this additional factor is manufactured elsewhere in the body. This aspect requires further experimental study.

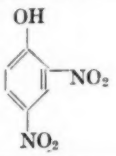
In order to test the possibility that the cataract may be due to dehydration, distilled water was instilled at frequent intervals during the period of poisoning; this, however, did not inhibit the development of cataract. If lenses after development of the opacities were removed and immersed in Ringer's solution of varying dilutions, the opacities cleared partially within a few hours, but this clearing process was not more marked in the lesser concentrations than it was in the higher salt concentrations. There is, then, no evidence that the cataract is produced by dehydration due to increased tonicity of the surrounding fluids.

With the peroral or intramuscular technique of administration, 37 compounds chemically related to dinitrophenol were tested in varying amounts for their cataract-producing capacity. With many of these compounds, the rectal temperatures of the chicks were recorded for several hours after poisoning, and the oxygen consumption of the animals was recorded in a respiration chamber after Tainter and Rytand.[7] The respiration chambers were kindly loaned by Dr. E. K. Marshall, Jr., department of pharmacology of the Johns Hopkins Medical School. The results are summarized in the following tables.

The following groups of compounds were tested and classified according to the modification of radicals attached to the benzene ring.

TABLE 1

GROUPS OF COMPOUNDS TESTED AND CLASSIFIED



2,4-DINITROPHENOL

I

IMPORTANCE OF PRESENCE, NUMBER AND POSITION OF *NITRO-GROUPS:*

Other DN-Phenols
Mono-Nitrophenols
Halogen-Phenols
Carboxy-Phenols (Salicylic Acids)
Aminophenol

II

IMPORTANCE OF PRESENCE AND NUMBER OF FREE *PHENOLIC HYDROXYL-GROUPS:*

Benzenes and DN-Benzenes
DN-Chlorobenzene
DN-Toluene
DN-Anisole
DN-Phenetole

III

INTRODUCTION OF SECOND *RING-SYSTEM:*

DN-Naphthol
DN-6-cyclo-hexyl-phenol

IV

INTRODUCTION OF *ADDITIONAL NITRO-GROUP OR HALOGENS:*

Picric Acid
2,4-DN-Chlorophenols

V

IMPORTANCE OF *METHYL- AND OTHER ALKYL-GROUPS:*

DN-Cresol
DN-Thymol
DN-tertiary butyl-phenol
DN-Mesitylene

VI

OTHER CYCLIC COMPOUNDS:

Naphthalene
Nitro-Cinnamic Acid

Summary of Table 2

Table 2 illustrates that any ommission or substitution of any of the two nitro-groups by either halogens or carboxyl-groups abolishes cataract-producing activity with the exception of 2,6-dibromo, 4-nitrophenol; that is, of a compound where one nitro-group in paraposition is maintained in addition to two halogens in ortho-position to the phenolic hydroxyl-group. It is of interest that 2,6-dinitro-4-chlorophenol—that is, a compound with two nitro-groups in ortho-position and one halogen in para-position—seems to be less active, although the higher general toxicity makes it difficult to draw very definite conclusions.

Shifting of the second nitro-group from para-position into ortho-position in 2,6-dinitrophenol reduces activity considerably.

It is obvious that the optimal situation is the presence of two nitro-groups, one in ortho-, the other in para-position, and that the presence of one nitro-group in para-position is of greater importance than the one in ortho-position.

Summary of Table 3

Omission or substitution of the phenolic hydroxyl-group by a halogen or methyl-group abolishes cataract-producing activity. The presence of the phenolic hydroxyl group is an absolute necessity. The activity of the anisole- and phenetole-compounds is most likely to be explained by an hydrolysis of the ester with liberation of the free phenol in the body; the somewhat delayed onset of cataract after administration of these compounds is in agreement with this interpretation.

Summary of Tables 4 and 5

Introduction of a second ring system into the molecule interferes with cataract-producing activity.

TABLE 2

IMPORTANCE OF PRESENCE, NUMBER AND POSITION OF NITRO-GROUPS
(First Part)

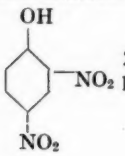
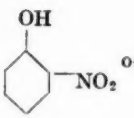
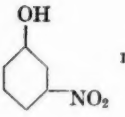
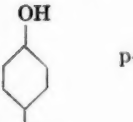
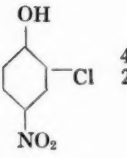
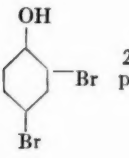
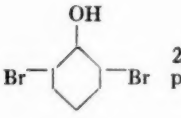
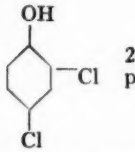
Compound	Amount millimol/kg	Application po:peroral im:i.muscul. o:in oil	Cataract in vivo	Onset of cataract hrs.	Death	Time of death hrs.	Cataract after death	Temper.—Drop more than 2° F.	Increase of O_2—Uptake
 2,4-dinitrophenol	0.03	po.o.	−	−	−			+	
	0.06	po.o.	+	3½	−			+++	
	0.11	po.o.	++	2	−			+++	
	0.11	im.o.	++	2	−				
	0.22	po.o.	++	1	±	24		+	
	0.43	po.o.	+	1	++	3			+
	0.43	im.o.			+	1	+		
 o-nitrophenol	0.71	po.o.	−	−	−				
 m-nitrophenol	1.00	po.o.	−	−	−				
 p-nitrophenol	0.86	po.o.	−	−	−				
	2.88	po.o.						−	
	5.76	po.o.	−	−					
	6.47	po.o.	−	−	+	1	+?		
 4-nitro-2-chlorophenol	0.81	po.o.	−	−	−				
 2,4-dibromophenol	0.32	po.o.	−	−	−				−
	0.56	po.o.	−	−	−				
 2,6-dibromophenol	0.56	po.o.	−	−	−				
 2,4-dichlorophenol	0.86	po.o.	−	−	−				−

TABLE 2

IMPORTANCE OF PRESENCE, NUMBER AND POSITION OF NITRO-GROUPS
(Second Part)

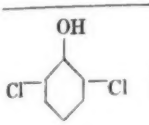
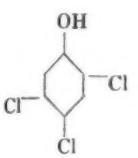
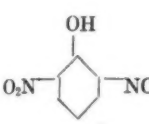
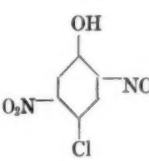
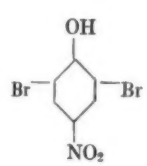
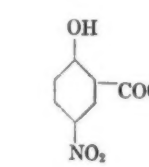
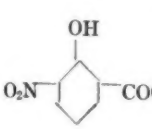
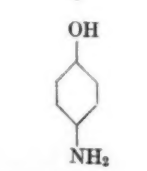
Compound	Amount millimol/kg	Application po:peroral im:i.muscul., o:in oil w:in water	Cataract in vivo	Onset of cataract hrs.	Death	Time of death hrs.	Cataract after death	Temper.—Drop more than 2° F.	Increase of O_2—uptake
 2,6-dichloro-phenol	0.74	po.o.	–	–	–				
 2,4,5-tri-chloro-phenol	0.31 0.41 0.31	po.o. po.o. im.o.	– – –	– – –	+	24		–	–
 2,6-dinitro-phenol	0.43	po.o.	±	5	+	5		+	–
 2,6-dinitro-4-chloro-phenol	0.18 0.37 0.55	po.o. po.o. po.o.	–	–	+ +	2 1	±? –		
 2,6-dibromo-4-nitro-phenol	0.13 0.27	po.o. po.o.	+ +	3 2	– +	 24		 +	 +
 3-nitro-salicylic acid	0.77	po.o.	–	–	–				
 5-nitro-salicylic acid	0.77	po.o.	–	–	–				
 p-amino-phenol (hydrochlor.)	0.84	po.w.	–	–	–				

TABLE 3

IMPORTANCE OF PRESENCE AND NUMBER OF FREE PHENOLIC HYDROXYL-GROUPS

Compound	Amount millimol/kg	Application po:peroral im:i.muscul o:in oil	Cataract in vivo	Onset of cataract hrs.	Death	Time of death hrs.	Cataract after death	Temper.—Drop more than 2° F.	Increase of O_2—uptake
m-dinitrobenzene	0.48	po.o.	–	–	±	24			
bromobenzene	1.02	po.o.	–	–	+	24			
iodobenzene	1.18	po.o.	–	–	–				
p-dibromobenzene	0.42	po.o.	–	–	–				
p-dichlorobenzene	0.82 0.82	po.o. im.o.	– –	– –	– –				
2,4-dinitrochloro-benzene	0.59	po.o.	–	–	±	24			
2,4-dinitrotoluene	0.77	po.o.	–	–	–				
2,4-dinitroanisole	0.40 0.40	po.o. im.o	+ +	5 4					
2,4-dinitrophenetole	0.38 0.38	po.o. im.o.	+ +	2 2	±	5			

TABLE 4

INTRODUCTION OF A SECOND RING-SYSTEM

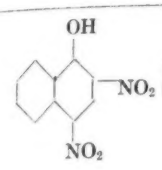
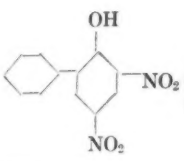
Compound	Amount millimol/kg	Application po:peroral im:i. muscul. o:in oil	Cataract in vivo	Onset of cataract hrs.	Death	Time of death hrs.	Cataract after death	Temper.—Drop more than 2° F.	Increase of O_2—uptake
 2,4-dinitro-naphthol	0.34	po.o.	−	−	+	4	−	+	
 2,4-dinitro, 6-cyclohexyl-phenol	0.22 0.22 0.30	po.o. im.o. po.o.	− − −	− − −	+ +	1 20 min.	± 	 +	

TABLE 5

INTRODUCTION OF ADDITIONAL NITRO-GROUP OR HALOGENS

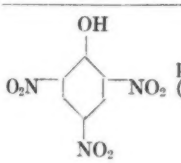
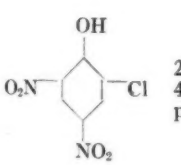
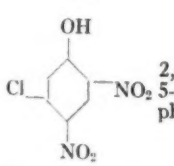
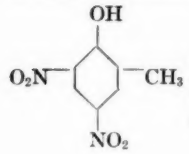
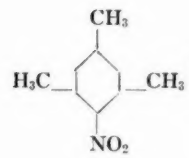
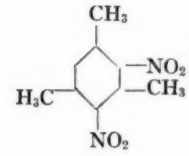
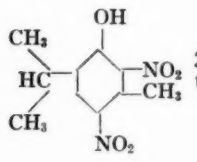
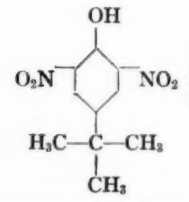
Compound	Amount millimol/kg	Application po:peroral im:i.muscul., o:in oil w:in water	Cataract in vivo	Onset of cataract hrs.	Death	Time of death hrs.	Cataract after death	Temper.—Drop more than 2° F.	Increase of O_2—uptake
 picrate (sodium)	1.75 (acid)	po.o.	−	−	+	2½	+		
	1.96 (salt)	po.w.	−	−	−				
	3.54 (salt)	po.o.	−	−	+	1	−		
 2-chloro-4,6-dinitro-phenol	0.28	po.o.	+	4				+	−
 2,4-dinitro-, 5-chloro-phenol	ab. 0.37	po.w.	−	−	−				
	0.73	po.& im.w.	+	¾ (45 min.)				+	+

TABLE 6

IMPORTANCE OF METHYL—AND OTHER ALKYL—GROUPS

Compound	Amount millimol/kg	Application po:peroral o:in oil	Cataract in vivo	Onset of cataract hrs.	Death	Time of death hrs.	Cataract after death	Temper.—Drop more than 2° F.	Increase of O_2—uptake
 3,5-dinitro-o-cresol (4,6-dinitro-o-cresol)	0.0125	po.o.	+	4–5	−			+	
	0.02	po.o.	+	2	−				
	0.025	po.o.	+	2	+	11½		+	+
	0.10	po.o.	+	1					
	0.30	po.o.			+	1	+		
 nitro-mesitylene	0.85	po.o.	−	−	−				
 2,4-dinitro-mesitylene	0.67	po.o.	−	−	−				
 2,4-dinitro-thymol	0.25	po.o.	−	−	+	3	+		
 2,6-dinitro-4-tertiary butyl-phenol	0.33	po.o.	−	−	deep anes-thesia			+	

Introduction of a third nitro-group in ortho-position seems to interfere with cataract-producing activity, although the experiments with picrate may not be quite conclusive in view of the general toxicity. Introduction of a halogen-group in addition to the two nitro-groups does not abolish activity, but reduces it to some degree.

SUMMARY OF TABLE 6

Introduction of one methyl-group in ortho-position increases activity about five-fold. However, introduction of addi-

TABLE 7

OTHER CYCLIC COMPOUNDS

Compound	Amount millimol/kg	Application po:peroral o:in oil	Cataract in vivo	Onset of cataract hrs.	Death	Time of death hrs.	Cataract after death	Temper.—Drop more than 2° F.	Increase of O_2—uptake
Naphthalene	61.54	po.o.	−	−	+	4			
p-nitro-cinnamic acid	1.04	po.o.	−	−	−				

tional methyl-groups and more complex alkyl-side-chains interferes with the cataract-producing activity.

SUMMARY OF TABLES 7 AND 8

The absence of any cataract-producing activity of naphthalene in acute experiments in the chick is of interest and will be referred to again in the discussion on the specificity of the effects of dinitrophenol.

Table 8 summarizes the approximate relative cataract-producing activities of various compounds of the previously discussed groups.

TABLE 8

COMPARISON OF CATARACT PRODUCING ACTIVITIES OF VARIOUS NITRO-COMPOUNDS (2,4-Dinitrophenol = 1)

4,6-DN-Cresol	4.8
2,4-DN-Phenol	1.0
2,4-DN-Anisole	≧0.5
2,4-DN-Phenetole	≧0.5
2,6-Dibromo-4-Nitro-Phenol	≧0.5
2-Chloro-4,6-DN-Phenol	≧0.22
2,4-DN-5-Chloro-Phenol	<0.16>0.08
2,6-DN-Phenol	0.14
m-DN-Benzene Mono-Nitro-Phenols 2-Chloro-4-Nitro-Phenol 2,4-DN-Naphthol 2,4-DN-Thymol Nitro-Salicylic Acids 2,4-DN-Chlorobenzene 2,4-DN-Toluene 2,4-DN-Mesitylene 2,4-Dichloro-Phenol	<0.125 or 0

DISCUSSION

1. SPECIFICITY

The absence of any cataract-producing effect of naphthalene in very high concentrations in these acute experiments and the loss of activity with even much slighter modifications in the molecule indicates that the cataract due to D.N.P. is a very specific phenomenon. Therefore, it appears very doubtful that the pathogenesis of cataracts, both clinical and experimental, reported in poisoning with various cyclic compounds has much in common with the mechanisms primarily concerned in D.N.P. cataract.

2. RELATION TO OTHER BIOLOGIC EFFECTS

Various nitro- and other substituted phenols, notably halogen-phenols, have

been extensively studied by Krahl and Clowes [8, 8a] in their effect on mitosis and metabolism in the eggs of some marine animals. The interference of halogen substitution and ring-system substitutions with cataract-producing activity is in strong contrast to these effects on marine eggs where both mitosis and respiration are similarly affected by nitro-phenols and by halogen- and some double-ring-phenols. This lack of correlation again underlines the high specificity we have to assume for the mechanisms involved in D.N.P. cataract.

The drop of body temperature found in chicks which had been poisoned with cataract-producing nitro-phenols has also been found with compounds which did not produce cataract and may be ascribed to other unrelated toxic effects of these compounds. Moreover, adult chickens did not show a drop in temperature, and it can, thus, be excluded that the cataract is a cold-cataract or otherwise closely or directly related to the body temperature changes.

A fairly good correlation was found between the cataract-producing activity and the metabolic effects on the whole animal of various compounds as tested by the basal metabolism. With at least two compounds, 2,6-D.N.P. and 2-chloro, 4,6-D.N.P., no increased metabolic rate was found in chicks in spite of the production of cataracts. It has to be admitted, however, that with these compounds the onset of cataract was delayed and that the difference as compared with other compounds may turn out to be only a question of dosage, if this could be tested without entering the ranges of general toxicity. At any rate, these two exceptions are not sufficient to justify the conclusion that the increased oxygen uptake does not have some relation to the cataract. It is quite conceivable that an increased oxygen uptake of the tissue is not the cause of the cataract, but rather a corollary, secondary effect of some primary metabolic disturbance and that a further set of unknown factors determines whether the oxygen uptake is increased in the tissue with no production of cataract, or cataract is produced without an increase in oxygen uptake, or whether both effects take place. It is of some interest in this connection that Field II, Tainter, Martin, and Belding[9] found an increased respiration in rabbits' lenses with certain concentrations of D.N.P., while it is known that this species is not susceptible to D.N.P. cataract.

The notion that the increased respiration is not the cause and is only indirectly connected with the cataract mechanism can easily be reconciled with a recent viewpoint held by biochemists on the mechanism of action of D.N.P. in tissue metabolism. It has been found that D.N.P. interferes vigorously with the phosphorylative processes in microörganisms;[10] the viewpoint based on these experiments is that increased respiration is only secondary to these disturbances in phosphorylative mechanisms and that, with this increased oxidation, energy is wasted and sidetracked from storage and utilization in high-energy phosphates which are connected with some specific tissue functions.[11] Experiments designed to test phosphorylative mechanisms in chick lenses with these various compounds and to correlate them to their respective cataract-producing activities would seem to be a promising experimental approach.

Summary

1. Acute reversible cataracts can be produced in chicks and chickens of any age within 1 to 1½ hours after application by stomach tube or by intramuscular injection of small amounts of 2,4-dinitrophenol in peanut oil. The threshold

dose is about 0.06 millimol per kg. body-weight.

2. In ordinary feeding experiments spontaneous recovery takes place; that is, the lenses clear again, in spite of continued presence of the drug in the diet.

3. Experiments to produce D.N.P. cataract in vitro have failed.

4. Thirty-seven chemically more or less closely related compounds have been tested for their cataract-producing activities. Of these, only eight produced cataracts in vivo within from 1 to 5 hours after administration, 3,5-dinitro-o-cresol (4,6-dinitro-o-cresol in another nomenclature) being the most efficient one with an activity about five fold that of D.N.P. itself. The most outstanding properties favoring cataract-producing activity are the presence of a phenolic hydroxyl-group, and of at least one nitro-group, preferably in para-position, while the addition of a second ring abolishes activity.

5. The cataract is not a cold-cataract nor an osmotic cataract due to dehydration.

6. A fairly close, but not absolute, correlation exists between the cataract-producing properties of these compounds and their ability to raise the basal metabolism of the animal. The possibility is discussed that an increased tissue respiration is only a corollary effect, and that the cataract is more directly related to other metabolic effects of these nitro-compounds and not caused by the increased respiration.

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Discussion

Dr. Clyde A. Clapp (Baltimore, Maryland): I should like to ask Dr. Buschke if he considers a reversible opacity in the lens as a true cataract or simply an opacity in the lens?

Dr. Wilhelm Buschke (New York): Well, I think that depends on the definition of the word "cataract." From a patho-physiologic standpoint, I think the essential thing is the change which takes place in the optical properties of the lens. As long as we don't know more about the pathogenesis of cataracts we had best stick to a definition based on this criterion, but for our purpose it doesn't matter much whether we call it "cataract" or "lens opacity."

Now, the interesting point in this type of lens opacity is that in various species it behaves differently. In human beings, it is not reversible; while in the animal it is. This raises the question whether this experimental cataract can be considered as analogous to the clinical cataract produced with this compound in human beings. I believe, however, it would be very far-fetched to assume that lens opacities produced by compounds of this type, both clinically and in experimental animals, would have nothing to do with each other, even if they follow a different course in different species.

Dr. Clapp: I should also like to ask Dr. Buschke what the difference is between a transparent protein and one which is opaque—for instance, what is the difference between clear proteins and precipitated proteins? Is it a chemical change or is it a physical change, with the rearrangement of the molecules or the atoms.

Dr. Verhoeff (Boston, Massachusetts): Does that have anything to do with this particular paper?

Dr. Clapp: I should think that any change in opacity is part of any change in the lens itself.

Dr. Verhoeff: Well, if Dr. Buschke would like to answer it, all right.

Dr. Buschke: I should be very happy if I could answer this question in relation to the lens because then, I think, the cataract problem would be solved; but I do not claim to have solved this problem.

Dr. Verhoeff: Most of us here are clinicians and I think we always try to apply everything clinically as far as possible. Perhaps that is not the correct attitude, but we all have it. I should like Dr. Buschke to tell us whether he has attempted to correlate his experimental work with the dinitrophenol cataract of human beings; for instance, does he think that every human subject would develop this cataract if the dose were sufficient? Or are certain individuals susceptible and others not? I don't know whether or not Dr. Buschke's experiments could be expected to cover that.

Dr. Buschke (closing): I think this is a very interesting and intriguing question. Of course, my experiments do not provide any direct answer to this question. However, according to Horner only a very small percentage of human beings, who have ingested the drug, do get cataract, and the occurrence of the cataract in human beings is correlated neither to the amount of drug nor to the period over which it has been taken. It appears, both on the basis of clinical observations and by virtue of the fact that—in contrast to human beings—these compounds produce lens opacities with about 100 percent regularity in some other species, that a genetic predisposition plays an important role in the susceptibility to this cataract.

VIRUS STUDIES IN LYMPHOMATOID DISEASES OF THE OCULAR ADNEXA

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INTRODUCTION

The possibility of viruses causing neoplasms is not a new concept. Borrel[1] suggested that cancer was the result of virus infections. Since then investigators in France and elsewhere have found neoplasms containing viruses. The hypothesis of the virus etiology of cancer has had a rather stormy course, and the majority of cancer-research groups refuse to consider it as a possibility. Duran-Reynalds and Shrigley[2] have compiled a large bibliography on the virus approach to the cancer problem.

Several general and ophthalmic pathologists have considered the possibility of some inflammatory diseases becoming neoplastic; this has been particularly true in the syndrome known as pseudotumor of the orbit. Biopsies of this peculiar orbital disease histologically show chronic inflammatory tissue. Similarly there has always been considerable confusion among these inflammatory tumors, lymphomas, and malignant exophthalmos associated with hyperthyroidism.

Birch-Hirschfeld[3] classified most of the types of orbital tumors, particularly pseudotumors. He classified the pseudotumors of the orbit as follows: (a) exophthalmos which regresses spontaneously, (b) exophthalmos associated with a definite orbital tumor that is relieved by removal of the tumor, and (c) exophthalmos which persists. Occasionally these pseudotumors of the orbit continue to extend and eventually a diagnosis of malignant lymphoma is made; although numerous associated lymph nodes may develop over the rest of the body, most of these individuals do not follow the usual course of a malignant lymphoma.

The present investigation was undertaken in order to determine the etiology of this particular type of malignant exopthalmos.

CASE REPORT

HISTORY

J. W. B. was first examined by numerous physicians in Glasgow, Scotland, in August, 1938, because of edema of the lids and conjunctivitis. Behind the upper lid was a palpable mass, and there was some exophthalmos of both eyes. The upward rotation of the right eye was limited; diplopia was present in this field and at times in the primary position. He gave a history that the swelling in the upper lids began insidiously in May, 1937. At that time it was thought that the swelling was allergic.

In October, 1938, two portions of the growth were excised by Professor Ballantyne. Sections of the tumor suggested a probable giant follicular lymphoma. X-ray studies of the chest was normal, and the vision at that time was 6/3 in each eye. The patient was given a course of X-ray therapy during which time his exophthalmos increased so that approximately six months later it measured 25 mm. in each eye.

VISUAL EXAMINATIONS

In May, 1939, he developed marked chemosis of the bulbar conjunctiva. The

* From the College of Physicians and Surgeons, Columbia University. Read at the 16th scientific meeting of the Association for Research in Ophthalmology, Inc., Atlantic City, June 10, 1947. This work was supported in part by a grant from the Snyder Ophthalmic Foundation.

vision was reduced to 6/9 in each eye. The differential blood count showed a marked eosinophilia, there being 14-percent eosinophiles with 61-percent neutrophiles; the lymphocytes were only 18 percent. A biopsy of the conjunctival tissue was performed, and the diagnosis of possible lymphocytoma was made. There were large numbers of eosinophiles present in the conjunctival tissue. The patient was given another course of X-ray therapy but with little improvement; the exophthalmos continued and by June, 1939, it had increased so that the apex of the cornea measured 33 mm. in each eye from the lateral rim of the orbit.

Fig. 1 (Braley and Alexander). These pictures of J. W. B. show the progress of the disease. The first was taken in September, 1938; the second in May, 1940; and the third in September, 1943.

He was again seen in March, 1940, and the eyes were more divergent; the interpupillary distance measured 71 mm.; the vision was reduced to 6/13 in the right eye and 6/36 in the left eye. The exophthalmometer reading was 31 mm. in the right eye and 36 mm. in the left eye. He was given repeated X-ray treatments, and the condition seemed to relapse so that by January 1, 1942, his vision had improved to 6/6 in each eye and the exophthalmos had decreased. However, by February, 1942, there was loss of vision, and the patient had many areas of degeneration in the fundi; it was noted that he also was developing cataracts.

By September, 1942, the vision was reduced to 3/60 in the right eye and 6/24 in the left eye. The exophthalmos was still marked. In November, 1942, a right frontal osteoplastic craniotomy was performed and the roof of the orbit was removed. Considerable orbital tissue was excised. Microscopic examination of the tissue showed a tumor of the myeloma group, probably plasmocytoma. However, the cells varied in type, and the muscles and connective tissue contained many eosinophiles and plasma cells. He was seen again a month later with marked ulceration of both corneas. The exophthalmos seemed to be greater than before the operation. By January, 1943, the eosinophilia had increased to 44 percent and the neutrophilic polys were 47 percent.

The patient was not seen for the next 2½ years but the proptosis continued and he developed bilateral cataracts. He was next seen in July, 1946, by Dr. A. B. Reese, whose examination revealed an extreme exophthalmos of both eyes which could not be measured with the exophthalmometer. Both eyes were fixed, the right eye turning down and out. There was edema and protusion of the bulbar conjunctiva of the lower lids with hyperkeratosis. In both orbits, firm nodular tissue was palpable through both the upper and lower lids. There were bilateral cataracts, and the right cornea showed extensive vascularization below, apparently due to exposure. There were tremendous tortu-

ous blood vessels in the lower fornix of the right eye. There were large lymph nodes in both sides of the neck extending into the cervical region.

It is interesting to note that on only three occasions was there any remission in the exophthalmos. This was during and following a severe bronchial pneumonia, for a short time after the craniotomy, and after an attack of pleurisy. On each occasion the exophthalmos returned.

Physical examination

The patient's blood pressure was 126/90 mm. Hg; the physical examination except for the head, neck, and eyes was essentially negative. There was an advanced exophthalmos with marked edema of the lids. There were numerous lymph nodes in the submaxillary region and many lymph nodes in the anterior and posterior cervical triangle. The parotids also appeared to be swollen, but there was no preauricular lymph node palpable.

The skin test with tuberculin was slightly positive in 1:100,000 dilution; however, when this test was repeated with 1:10,000 dilution it was entirely negative. The Frei test was negative, the brucellergyn test was positive, and the blood Kline was negative. The blood count showed 11.6 gm. of hemoglobin, 3,850,000 erythrocytes, and 8,400 leukocytes. The sedimentation rate was elevated by 101 mm. in one-half hour and 127 mm. in one hour. There was 45-percent neutrophiles, 20-percent eosinophiles and 34-percent small and large lymphocytes. The metabolic rate was +15, but this reading was not reliable. There was diffuse clouding in the X-ray pictures of the sinuses. Repeated blood counts showed a definite eosinophilia ranging between 20 percent and 24 percent. X-ray studies of the chest showed definitely enlarged hilar lymph nodes; and the blood agglutination for brucella was positive up to 1:320. Blood cholesterol was normal and the A/G ratio was 0.2. There were no changes in the long bones or in the joints in the hands. Fasting blood sugar was 83 mg. percent and the blood-sugar curve was normal. The cephalin flocculation was negative. Serum phosphatase was 1.4 Bodansky units. The urea-nitrogen was 16 mg. percent.

A biopsy of the left submaxillary gland and several lymph nodes was done since the patient did not wish to have his orbits reëxamined. There was considerable confusion in the diagnosis of the tumor. It was considered a giant follicular lymphoma by the majority of pathologists, but Dr. A. P. Stout thought the tissue inflammatory and not neoplastic.

Pathology of clinical disease

A microscopic slide made from the original biopsy of the orbit was available for examination. The section shows an elongated piece of tissue on one side of which a small bit of glandular material is seen. The gland appears to be part of the lacrimal or accessory lacrimal gland. The tissue is composed mostly of dense strands of connective tissue. Interposed between these strands are collections of lymphocytes.The connective tissue is also lightly infiltrated with lymphocytes. The masses of lymphoid tissues are in general similar; they are composed of small and large lymphocytes at the periphery of the masses and, near the center, the lymphocytes become paler and suggest a germinal center. These central areas are composed of pale, blue-staining cells in which an occasional mitotic figure is present. There is also an occasional eosinophilic cell in these masses. The tumor has the general appearance of a giant follicular lymphoma.

The lymph nodes and submaxillary gland from which the animal inoculations

were made were also available for histologic examination. The lymph node has lost most of its normal markings. The sinusoids are densely infiltrated and there are no definite lymph follicles with germinal centers seen. The entire lymph node is generally infiltrated with lymphocytes. The normal architecture of the hilar area is obliterated because of the lymphocytes.

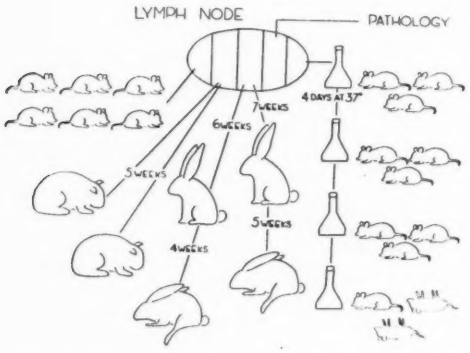

Fig. 2 (Braley and Alexander). Experimental studies showing the marked infiltration with lymphocytes.

Most of these lymphocytes are mature; there are a few cells that simulate lymphoblasts scattered in the lymph node and an occasional plasma cell. There are also a few plasma cytoids and Russell bodies present. Under the oil-emersion lens, most of the larger cells appear to be endothelial cells from the lymph sinusoids, and some of these cells appear to be degenerated. Some of the cells are multinucleated simulating Dorothy-Reed cells. An occasional eosinophile is present. The submaxillary gland is densely infiltrated with lymphocytes so that the glandular tissue is spread apart by the collections of lymphoid elements. It is composed more of lymphoidal tissue than of normal glandular tissue. The lymphoidal tissue here is likewise composed largely of adult lymphocytes. There may be a few more eosinophiles present in the submaxillary gland than in the lymph node. An occasional plasma cell and a few plasma cytoids are present. Some of the cells which appear to be large lymphocytes show clear spaces in the nucleus which could represent nuclear inclusions, but these are indefinite. Some of the collections of lymphocytes appear to have germinal centers.

Methods of study

A large lymph node and several pieces of the submaxillary gland were available for study. The tissue was divided into six parts. One part of each section was studied histologically; some of the tissue was placed in the deep freeze and other material was macerated in balanced salt solution. Two types of tissue culture were inoculated with this material. One type consisted of serum ultrafiltrate, balanced salt solution, and finely-divided embryo mouse brain, similar to the procedure followed by Simms and Sanders[4] for propagation of lymphogranuloma virus. The other type of tissue culture was similar except that 17-percent sterile horse serum was substituted for the serum ultrafiltrate. This latter type of tissue culture maintained a more normal pH without adjustment with carbon dioxide as is required with serum ultrafiltrate. All of the inoculated tissue cultures were carried at incubator temperature (37°C.).

These tissue cultures were subinoculated at varying intervals of from 4 to 6 days, then inoculated intracerebrally and intraperitoneally into mice. The original tissue cultures were reinoculated into fresh tissue cultures when the mice were inoculated. The inoculated mice were followed for periods of from 4 to 6 weeks before they were discarded. As the tissue cultures increased in number, each series was inoculated intracerebally and intraperitoneally into mice. After five consecutive passages through tissue cultures, two of the six mice inoculated

showed signs of encephalitis. Their brains were removed and passed in tissue cultures and other mice. Subsequently a potent agent was obtained, and this procedure of inoculation from tissue culture to mice has been carried on for 28 consecutive passages. During this process, the potency of the virus gradually increased so that it was necessary to make serial dilutions of the tissue culture before the test mice could be inoculated. The tissue-culture potency of the virus was raised to 10^{-6} when tested by serial dilutions intracerebrally in mice. The highest potency of the virus obtained in tissue culture was after four days at incubator temperature.

At the same time that the original tissue cultures were inoculated, the glandular tissue was also macerated in balanced salt solution and inoculated intracerebrally into two guinea pigs, two rabbits, and six mice. The first rabbit developed paralysis of the hind legs 22 days after inoculation; the rabbit lost weight and became lethargic. When it was apparent that the rabbit was ill with an encephalitis, it was killed and the brain removed. The entire brain was stored at −50°C. The second rabbit developed similar symptoms 35 days after inoculation; this brain was also removed and stored at −50°C. The rabbit brain was inoculated into tissue culture, intracerebrally and intraperitoneally into six mice, and intracerebrally into other rabbits. After eight days two of the six mice were dead. The first rabbit inoculated developed encephalitis in 10 days and the second in 12 days.

Of the two guinea pigs inoculated from the original material, the first developed symptoms in 23 days and the second in 32 days. They showed signs similar to the rabbit in that they became lethargic and developed slight paralysis of the hind legs. Their brains were removed and inoculated into other guinea pigs. When it was apparent that an agent was present which would produce an encephalitis in rabbits and guinea pigs, it was decided to inoculate some of the original tissue which had been kept at −50°C. This material was thus inoculated intracerebrally into guinea pigs and although it produced an encephalitis, the incubation period was prolonged to 42 days and 45

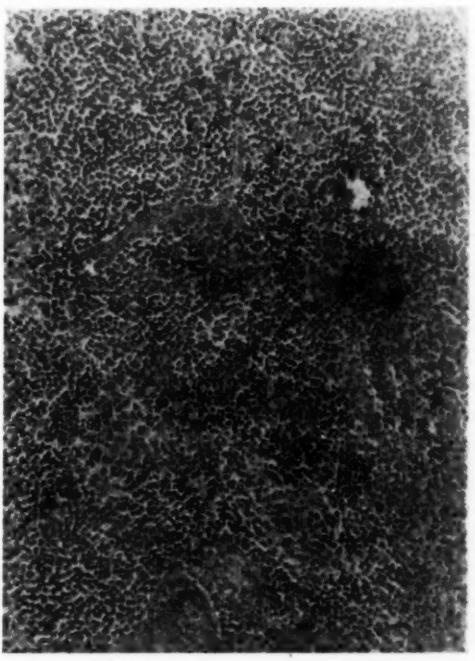

Fig. 3 (Braley and Alexander). Pathology of material for investigation. This shows the marked replacement of the submaxillary gland by lymphocytes.

days, respectively. Since this material appeared to be less virulent than the fresh tissue and was less virulent than the material already obtained in rabbit and mouse brain, it was decided to discontinue these studies.

The second intracerebral guinea-pig inoculation of brain suspension shortened the incubation period. The incubation period was decreased to 14 and 17 days, respectively. The intracerebral transmission into other guinea pigs was continued and again the incubation period was re-

duced; however, one guinea pig was encountered which did not develop symptoms until three months after inoculation. Four consecutive guinea-pig passages were done. Some of the guinea-pig brain was also used to inoculate tissue culture and eventually produced an encephalitis in mice.

Investigation was carried on for the most part with rabbits and mice, utilizing

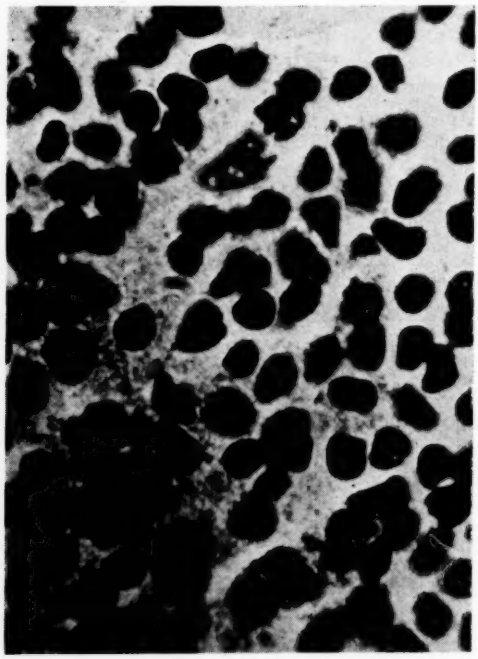

Fig. 4 (Braley and Alexander). Rabbit brain after inoculation with virus shows infiltration with lymphocytes.

tissue culture as an intermediate media to increase the potency of the virus. Six serial passages were carried out in rabbits. All the rabbits were inoculated in a similar manner. The inoculum consisted of a 1:10-dilution of rabbit brain suspension from the previous animal. This material was ground in a ball mill and sufficient balanced salt solution added to make the dilution. Adult rabbits were partially anesthetized with either inhalation ether or nembutal intraperitoneally, and a small trephine was made through the skull with a short sharp punch. The hair over the skull was shaved prior to the punch, and the entire area painted with iodine. A needle was then inserted into the brain and from 0.2 cc. to 0.5 cc. of this inoculum injected. Although the incubation period of the original material was approximately three weeks, the second rabbit developed symptoms in two weeks. In the third rabbit passage, the incubation period was reduced to one week, and from then on the incubation period did not seem to shorten materially. At each passage some of the rabbit brain was removed for mice- and tissue-culture inoculations. After the second passage in rabbits, 2 of 6 mice died from the direct rabbit-brain inoculation. The tissue culture from this brain was assayed in mice, but its potency was not increased. With each continual passage in rabbits, however, more mice in each series died from the intracerebral inoculation, so that after the fourth passage in rabbits, intracerebral inoculation of the rabbit-brain material produced encephalitis in all of six mice inoculated. After the fourth passage in rabbits, the rabbit-brain material was transmitted intracerebrally to guinea-pig brain and found to be highly potent, the incubation period being reduced to five days. In order to increase the potency of the virus one of the tissue cultures from the fifth passage in rabbits was passed at 5-day intervals. The potency in tissue culture gradually increased so that, when assayed in mice, it killed all of the mice inoculated.

During the early part of the experiments, mice were inoculated both intracerebrally and intraperitoneally. After the fifth passage in rabbit brain, only the intracerebral mouse inoculations were necessary to kill the mice. Because of the expense involved in continual passage in rabbits, we felt that six passages in rabbits were all that were necessary, since we

had the virus not only in rabbits but also in mice, guinea pigs, and tissue culture. By transferring the rabbit brain and mouse brain into tissue culture and back into mice, a very potent virus was obtained. In tissue culture a potency of 10^{-6} was present; in mice this was increased to 10^{-7}. Each of the isolations produced an identical virus.

Neutralization tests

Gordon,[5] in 1933, reported a successful transmission of Hodgkin's disease in rabbits. Ground Hodgkin's lymph nodes suspended in saline and injected intracerebrally in rabbits produced an encephalitis from which the rabbits eventually died. The symptoms that were obtained by Gordon were similar to those we found in rabbits. Gordon was unable to transmit the rabbit encephalitis to other rabbits. It was later shown by Turner, Jackson, and Parker[6] and again by McNaught[7] that intracerebral inoculation of esosinophiles would produce the same encephalitis in rabbits. Our agent, however, could be transmitted in rabbits, guinea pigs, and tissue culture.

When an agent is present in the body it usually stimulates the formation of antibodies. Therefore, one of the best methods of determining if a virus was obtained from an individual is to search for substances which will neutralize the virus. There are several methods of determining antibodies, but the easiest is to determine their presence in blood serum. It has been shown that after a disease has been present for a varying length of time antibodies are produced. One method of determining their presence is by mixing the virus with the blood serum and then testing for the presence of the virus. In order to arrive at a definite figure, it is necessary to determine the potency of the virus by serial dilutions. These dilutions are usually made in powers of 10. Each dilution is made so that when 0.02 cc. is injected intracerebrally in mice the actual dosage in mice is 1:10, 1:100, 1:1,000, 1:10,000, and so forth. These dilutions are, therefore, made by logarithmic power. The serial dilutions are then called 10^{-1}, 10^{-2}, 10^{-3}, and so forth, until a dilution is reached where the animals inoculated remain alive after inoculation. If a definite amount of blood serum is added to each of these dilutions so that subsequent dilution is the same as the control to which no serum is added, this can be used as a test to determine the presence or absence of neutralizing antibodies in the serum and the number of neutralizing antibodies when compared to the control. To determine the presence of antibodies each of the dilutions from 10^{-1} to 10^{-6} were injected intracerebrally into three mice, so that for each test 18 mice were used. If the serum completely neutralized the virus, then all the injected mice remained alive while the control mice died. If the serum partially neutralized the virus, then those with the lower dilutions of the serum-virus mixture died while those with the higher dilutions remained alive. This would then indicate a certain degree of antibodies.

Antisera were obtained which would neutralize the viruses of herpes simplex and epidemic keratoconjunctivitis. Normal rabbit serum, normal mouse serum, and several normal patients' sera were also analyzed; blood serum from the patient from whom the tissue had originally been obtained was tested. None of the known sera neutralized the virus; however, the patient's serum neutralized the virus in all dilutions up to 10^{-1}. With normal human sera, all mice were dead in dilutions up to 10^{-6}. Normal rabbit and mouse serum possessed no antibodies to the virus, and only one other patient was found who had any evidence of neutralizing substances in the serum.

Since the amount of serum needed from the patient in conducting neutralization tests was great, we thought it advisable to try to develop an antiserum in animals. Therefore, following a hyperimmunizing procedure, we injected rabbits intraperitoneally and intravenously with small amounts of the virus. Gradually increasing the amount of virus injected gives rise to high antibody titre in rabbits; the rabbit serum can then be used in neutralization tests. After intravenous inoculation with the virus, the rabbits gradually began to lose weight and, although we gave small quantities of the virus, we were unable to demonstrate antibodies in the majority of rabbits. During the intravenous inoculation, blood studies on the rabbits showed a marked increase in the number of lymphocytes. There was only a slight increase in blood count of the rabbits, but the lymphocytic count was as high as 90 percent. This was associated with a slight increase in the lymph nodes throughout the body, particularly those in the peripheral lymphatic system. X-ray studies of the chest and postmortem examination of the mediastinum failed to demonstrate a lymphadenopathy. One rabbit was finally obtained whose serum showed neutralizing antibodies. The antibodies that were present, however, only partially neutralized the virus. When rabbits were inoculated intracerebrally with small amounts of the virus so that the incubation period was prolonged to about three weeks, if they were bled during the first few days of their illness they showed some neutralizing antibodies. Usually these neutralizing antibodies did not develop above 10^{-4}.

In all the neutralization studies we have found only two patients who possess antibodies to the virus. One was the patient from whom we obtained the original material, and the second was a woman who had a peculiar lymphoma in the conjunctiva associated with numerous lymph nodes in the neck. Material was obtained from this patient for study but thus far no definite findings can be presented.

An attempt has been made to obtain serum from other types of lymphatic disease. Blood serum was obtained from four patients suffering from Hodgkin's disease. These patients were in various stages of Hodgkin's disease, and we feel that they should have had neutralizing antibodies if our virus was related to Hodgkin's. None of the patients' sera had any evidence of circulating antibodies to the virus.

Filtration experiments

Insufficient data has been collected on filtration to indicate the size of the virus, but enough has been done to show that the virus is small and passes most filters readily. The Seitz absorption-type filter passes the virus in low dilutions. Most of the gradacoll filters we have at hand pass the virus; it appears to pass the gradacoll filter with an average pore size of 93 millimicrons. No high-speed centrifugation experiments have as yet been done.

Attempts to reproduce the clinical disease

When the material is injected intravenously in rabbits, there is a gradual weight loss and in some of the rabbits there is a gradual lymphadenopathy. With the intravenous injection, there appears to be a marked increase in the number of white blood elements. In some instances actually there is a decrease in the white elements from 6,000 to 5,000. The normal white count in a rabbit varies from 3,000 to 7,000. After intravenous inoculation with the virus, the relative number of lymphocytes increases up to 90 percent. There are two possible explanations; either the virus destroys the leukocytic group leaving only the lymphocytic cells,

or the lymphocytes are increased at the expense of the leukocytic cells. The differential counts in rabbits range from 80 to 90-percent lymphocytes, while in normal rabbits the lymphocytic count is rarely over 50 percent. Most of the differential counts in normal rabbits show about 50-percent polymorphonuclear leukocytes and from 40 to 50-percent lymphocytes. In most instances after intravenous inoculation, there is some increase in the size of the lymph nodes. This is particularly pronounced in some of the rabbits; however, this finding seems to be inconsistent, and by intravenous inoculation it is not always possible to produce lymphadenopathy or consistent blood changes.

Single intraperitoneal inoculation into rabbits produces little change except on postmortem examination where there is an increase in the number and size of the lymph nodes. Retrobulbar inoculation of tissue culture containing the virus produces an exophthalmos which persists over a long period of time but gradually seems to decrease. The rabbits given retrobulbar inoculation, however, developed signs of an encephalitis and eventually died. They likewise showed enlargement of the spleen and the liver. The rabbits with the retrobulbar injection developed some neutralizing antibodies to the virus before death. To determine whether the virus produced the exophthalmos and eventual death of the rabbits, one rabbit was inoculated intraorbitally with normal tissue culture. Another rabbit was inoculated with tissue culture in which the virus had been grown for four days. Part of this culture was inoculated into the orbit and another part heated to 60°C. for one hour. This heated virus was also injected into the orbit. Neither of the latter two rabbits showed any symptoms of exophthalmos nor did they develop antibodies to the virus.

Pathology of the experimental disease

The liver, lungs, spleen, and lymph nodes were available for microscopic examination from rabbits which had been given the virus intravenously. The lymph nodes are enlarged but still show reasonably normal architecture. The sinusoids and the hilar region of the lymph nodes show some increase in the lymphocytic infiltration. There are quite a number of mitotic figures present in the lymph nodes, especially in the germinal centers. In some of the lymph nodes there are a few eosinophiles. The lungs show slight lymphocytic infiltration in the alveolar wall, but most of the lymphocytes are perivascular. The most striking change in the rabbit is in the liver where there is dense lymphocytic infiltration around the blood vessels at the periphery of the liver lobules. There are also lymphocytic infiltrations around the biliary capillaries. The spleen shows some increase in pigmentation and some evidence of increase in the amount of cellular debris but is otherwise normal.

The histologic examination of the rabbit brain which had been inoculated directly with the virus shows the most striking change. The arachnoid is densely infiltrated with lymphocytes. In spite of the fact that there is considerable thickening of the arachnoid and dense infiltration with lymphocytes, no polys are present. There is also considerable cellular debris in the arachnoid, and some of this debris is being phagocytized by large mononuclears. The brain substance in some areas is densely infiltrated with lymphocytes, particularly in the basal portions around the brain stem. Sections of the sixth passage of rabbit brain shows the most advanced pathologic processes. There is a moderate amount of death of brain cells, particularly the large ganglion cells. The cells are shrunken away from

the brain tissue and show some pyknosis. A few show small astrocytes around them.

Guinea pigs inoculated intraperitoneally showed some increase in the size of the lymph nodes. Histologically these lymph nodes show more changes than those found in the rabbit. The entire lymph node is densely infiltrated with lymphocytes, and the normal markings appear to be compressed. The entire area is densely infiltrated and some of the larger cells appear to be lymphoblasts. There is an occasional eosinophile in the sections. The spleen appears to be normal. The sections of the liver also show perivascular infiltration of lymphocytes at the periphery of the lobules.

Sections of mouse brain inoculated directly with the virus show similar pathologic processes to those seen in the rabbit. The lymphocytic infiltration of the arachnoid and pia is marked, but there is considerably more infiltration of the brain substance. This is particularly true around the ventricular spaces.

The pathologic condition of the animals studied demonstrates that the virus when inoculated into animals gives rise to a generalized lymphocytic infiltration no matter in what manner the virus is inoculated.

Discussion of the experimental data

Several pieces of tissue obtained from the submaxillary gland and adjacent lymph nodes were inoculated into tissue culture, mice, guinea pigs, and rabbits. The tissue culture was passed serially and eventually became infectious for mice. The intracerebrally inoculated rabbits developed an encephalitis, and their brains contained an agent which could be transmitted from one rabbit to another. With each passage the incubation period was decreased and the severity of the encephalitis increased. Six consecutive passages were accomplished in rabbits. The rabbit brain inoculated into tissue culture became infectious for mice. The original guinea pigs inoculated also developed encephalitis and the agent was successfully transmitted in guinea pigs three times. The substance present in guinea-pig brain, after passage in tissue culture, became infectious for mice.

The infectious agent when grown in tissue culture was transmitted to mice, rabbits, and to a lesser degree to guinea pigs. The potency of the agent in passage in mice had been increased to 10^{-7} dilution. The potency in tissue culture when tested in mice had been increased to 10^{-4}. When the virus was grown in tissue culture, the optimum requirement for highest titre was four days at 37°C. There was no visible change in the appearance of the tissue culture when the titre of the infectious agent was highest. We, therefore, obtained from the original tissue by three different methods an agent which produced identical symptoms in each test animal when passed from one to another.

Whenever an apparently new virus is discovered by animal inoculation, there is always a possibility that a latent virus was stimulated in the animal inoculated. There are several methods of determining whether the virus found was present in the animal inoculated. Most viruses have a definite host range. This is particularly true of Theiler's virus, which is usually picked up in the mouse and is noninfectious for rabbits and only slightly infectious for guinea pigs. The mice inoculated directly with this material did not develop symptoms. If the virus encountered had been Theiler's, herpes, or some other virus, the inoculation of mice would have immediately produced symptoms.

There was no evidence of neutralizing antibodies in normal rabbit blood, normal mouse blood, or normal guinea pig blood. Normal human serum also failed to neu-

tralize the virus. Only two human sera have been found that possess neutralizing antibodies to the virus—the patient from whom the original tissue was obtained and another individual who is suffering from a peculiar type of lymphoid disease. Our disease is probably not related to Hodgkin's or similar lymphoma since none of the serum tested from patients with these diseases possessed neutralizing antibodies.

The virus when inoculated intracerebrally into animals gave rise to an encephalitis in which the cellular reaction was entirely lymphocytic. When inoculated intraperitoneally and intravenously, there was an increase in the lymphocytic elements with a marked decrease in the leukocytic cells. The virus may destroy the leukocytes rather than increase the lymphocytes since there was no appreciable increase in the number of white blood elements present.

The virus could be one of the causes of pseudotumor of the orbit. It is known that in pseudotumor of the orbit many patients develop exophthalmos which persists for a long period of time but may spontaneously disappear with or without treatment. Some pseudotumors of the orbit persist for long periods of time and develop into a definite tumor with persistent exophthalmos. When these are removed, results are usually good. The third type of pseudotumor is, in some respects, similar to that of the patient presented here in that the tumor increases in spite of treatment and is histologically indistinguishable from some of the lymphomas. Whether the virus found in this patient has any relationship to the usual lymphoma has not been determined. From the blood-neutralization experiments, it would appear that the virus has no relationship to Hodgkin's disease. Insufficient data are at hand to determine this point at the present time. It may be that the virus can give rise to several types of lesions which vary from entirely benign to potentially malignantlike tumors so that when present in the lymphoid tissue it may give rise to a quasi-lymphoma.

An attempt is being made to isolate a virus from the only other patient who had neutralizing antibodies to the virus. The amount of material obtained from this patient was relatively small, and at the present time it is doubtful that we will recover a virus from this patient.

Conclusions

1. A preliminary report of a new virus is presented.
2. This virus was obtained from lymph nodes and submaxillary gland of a patient suffering from a type of malignant exophthalmos.
3. The virus produces an encephalitis in rabbits, guinea pigs, and mice and grows well in tissue culture.
4. The cellular response to the virus in animals is predominantly lymphocytic.
5. The virus is small in size and is submicroscopic.
6. The virus is neutralized by blood serum from the patient.
7. Normal human serum and the blood serum of most laboratory animals contain no neutralizing antibodies.
8. The virus has not been identified in any known classification.

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Discussion

Dr. F. H. Verhoeff (Boston, Massachusetts): I would like to ask what happened to the patient. What was the further course. Did he recover?

Dr. Alson E. Braley (New York): He was given X-ray treatments. When last heard from, his progress was satisfactory. Although he thought he was slightly improved, he had no vision in either eye and there was marked exophthalmos. He had been given a large number of X-ray treatments.

Dr. Verhoeff: Your explanation is that the case is one of an atypical pseudotumor.

Dr. Braley: Yes, sir.

Dr. Verhoeff: This might simply be one of the more severe cases. Some of these patients have much more resistance.

I also wanted to point out that at the time you first saw this patient there was a tremendous lymphoma and granuloma, and that you found what I think is a characteristic thing—a little lymphoid follicle, with profuse obliteration of the blood vessels.

Dr. Parker Heath (Boston, Massachusetts): I would like to ask a question. Do you classify this man as a case of real Brill-Shimmer's disease?

Dr. Braley: No, sir, I don't know how we should classify him. I have looked over all his slides from 1938 to the present time, and there is a tremendous variation in the microscopic appearance of the tumor. The first biopsy of the orbit looked like a giant follicular lymphoma, and as you can see from the last biopsy, it looks like an inflammatory lesion of the submaxillary gland and the lymph nodes. I think we might call some of these lesions quasi-lymphomas or lymphatoid lesions.

Dr. Verhoeff: Was there a lot of fibrosis in the last one?

Dr. Braley: Not so much in the last, but lots of fibrosis was present in the first biopsy.

Dr. Heath: This also enters the realm of the neuropotential, in the change in cells from one grade to another.

Dr. Verhoeff (closing): It is certainly refreshing to discover something from these pathologic processes. We try but we generally don't get anything.

CYANIDE INHIBITION OF CORNEAL RESPIRATION*

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Iowa City, Iowa

Metabolic processes in the cornea have not been extensively studied, even though this tissue is well adapted to experimental investigation. The importance of such information in contact-lens fitting, corneal transplantation surgery, and similar fields is obvious. The avascular nature of the tissue and the low rate of oxygen consumption might suggest that the respiratory mechanisms involved are of a different nature than those in other types of mammalian tissue. Yet preliminary studies indicate that the essential components of certain dehydrogenase and cytochrome systems are present.[1]

Inhibition of heavy metal catalysis by cyanide is a means of determining the activity of cytochrome oxidase in tissue respiration without disrupting the normal cellular structure. The drug is effective in low concentrations, is relatively specific in its action, and penetrates cell membranes readily. Herrmann, Moses, and Friedenwald[1] found that both cyanide and azide produced some inhibition of the intact bovine cornea, and that the addition of cytochrome-c to ground and dialyzed corneal tissue resulted in an increased oxygen uptake when hydroquinone or phenylenediamine were present as substrates. From these findings they concluded that the cytochrome system plays a part in the normal oxidative processes. Because the technique of controlling cyanide concentration in manometric experimentation has recently been improved[2] a more extensive study has been made to determine how much of the normal respiration may be depndent upon an iron-containing enzyme complex.

Methods

Respiration measurements were made with Warburg manometers at 37.5°C., using flasks of about 7-cc. capacity. Each flask received one cornea, cut in half to prevent folding, from a rabbit of 1½ to 3 kilograms weight. Unless otherwise indicated, 1.0 cc. of pH-7.4 Ringer-phosphate buffer containing 0.2-percent glucose[3] was added, and 0.6 cc. of 10-percent KOH solution or 10-percent $Ca(OH)_2$ suspension was placed in the center well on filter paper to absorb CO_2. In the experiments with cyanide, 0.1 cc. of neutralized KCN solution of 10 times the desired final concentration was added to 0.9 cc. of the buffer in the flask after the cornea had been added, and 0.6 cc. of the $Ca(CN)_2$-$Ca(OH)_2$ solution having an equivalent HCN tension[2] was placed on filter paper in the center well. In the experiments testing recovery from cyanide exposure the corneas were removed from the flasks at the end of the exposure period, rinsed in buffer, and returned to the washed flasks which now contained fresh fluid and center-well solution without cyanide.

Results are expressed in terms of dry weight. After each experiment, the corneas were rinsed in distilled water, laid on cover glasses, and weighed after drying to constant weight at 100° to 110°C.

Results and Discussion

There is a definite and consistent inhibition of corneal respiration by the higher concentrations of cyanide, as shown in Figure 1. The oxygen consump-

* From the Department of Ophthalmology, College of Medicine, State University of Iowa. Aided by a grant from the John and Mary R. Markle Foundation. Read at the 16th scientific meeting of the Association for Research in Ophthalmology, Inc., Atlantic City, June 10, 1947.

tion of the control tissue is constant for more than six hours, and the corneas in cyanide have constant rates also at levels

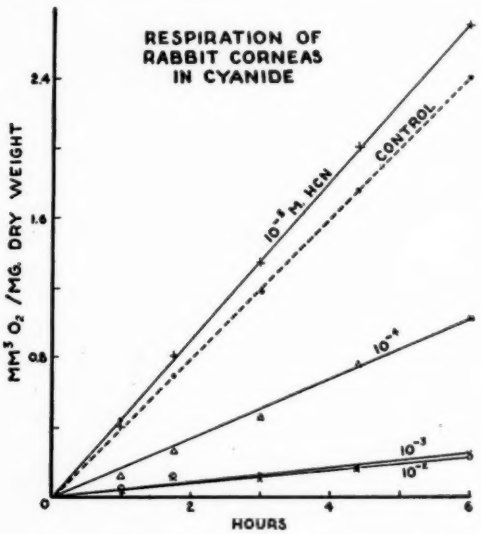

Fig. 1 (Robbie, *et al.*). Oxygen consumption of whole rabbit corneas in various concentrations of cyanide.

which vary with the HCN concentration. This variation with concentration is illustrated more completely in Figure 2, which shows the inhibiting effects of a range of concentrations from 10^{-2} to 10^{-6} M.

A 10^{-4} M. HCN produces about 50 percent inhibition of respiration, and 10^{-3} M. leaves a residual oxygen consumption of less than 10 percent. It is apparent that a cyanide-sensitive enzymatic system is responsible for most of the normal corneal oxygen uptake.

Riboflavin deficiency produces corneal vascularization in rats,[4] a finding which suggests that this vitamin is in some way involved in corneal oxidative metabolism. The riboflavin may play its part as a hydrogen carrier that is autoxidizable and reacts directly with molecular oxygen, or it may be used in a flavoprotein intermediate that serves as a connecting link between the dehydrogenases and the cytochrome system. If its main function were the former and if it were a highly active factor in corneal metabolism, one would expect the respiration of the tissue to be quite insensitive to cyanide. However, if its main role is that of an intermediary which interacts with the cytochrome system, the oxygen consumption should be blocked by cyanide. The latter scheme of action appears the more probable.

Recovery of respiration upon the removal of cyanide is rapid. By the time a cornea is washed, returned to the manometer, and reëquilibrated, recovery is almost complete. This is demonstrated by the experimental results presented in Figure 3. The cornea which was removed from the cyanide solution and washed after a 15-minute period of inhibition showed about the same oxygen uptake as the control (curve 1). The flask which was set up with HCN in the fluid but with KOH in the center well rather than a properly balanced alkali-cyanide mixture, lost HCN gas to the KOH so rapidly that again recovery was almost complete before a measurement could be made (curve 2). Pronounced inhibition occurred, however, when the center-well

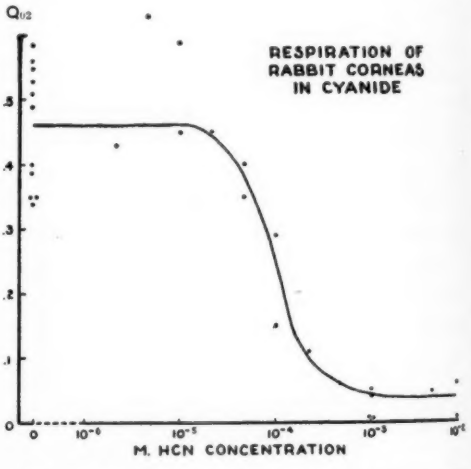

Fig. 2 (Robbie, *et al.*). Variation in corneal respiration with HCN concentration. Each determination is for a 2-hour measurement period.

solution had an HCN tension equivalent to that of the fluid in the flask (curve 4). The importance of maintaining the proper concentrations of HCN gas in the manometer flasks by the use of center-well solutions of equivalent HCN tensions is obvious.

The nature of the linkage between cyanide and the ferric iron in cytochrome oxidase is not definitely known. If the combination were stable, recovery would occur only as rapidly as new enzymes were formed. The evidence presented in the recovery experiments illustrated in both Figures 3 and 4 indicates that the union in this particular tissue at least is very labile, and that a constant tension of HCN gas must be maintained in the manometer flask to inhibit a constant portion of the respiration.

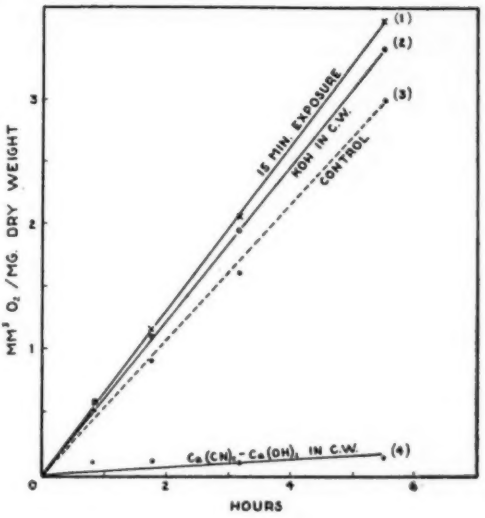

Fig. 3 (Robbie, *et al.*). Experiment demonstrating the importance of maintaining proper HCN equilibrium in manometric experiments. For explanation see text.

In manometric work with tissue slices the limiting thickness which still permits adequate oxygenation is determined by the rate of respiration of the tissue, the coefficient of diffusion of oxygen through the tissue, and the oxygen tension of the gas phase.[5] The cornea exceeds the maxi-

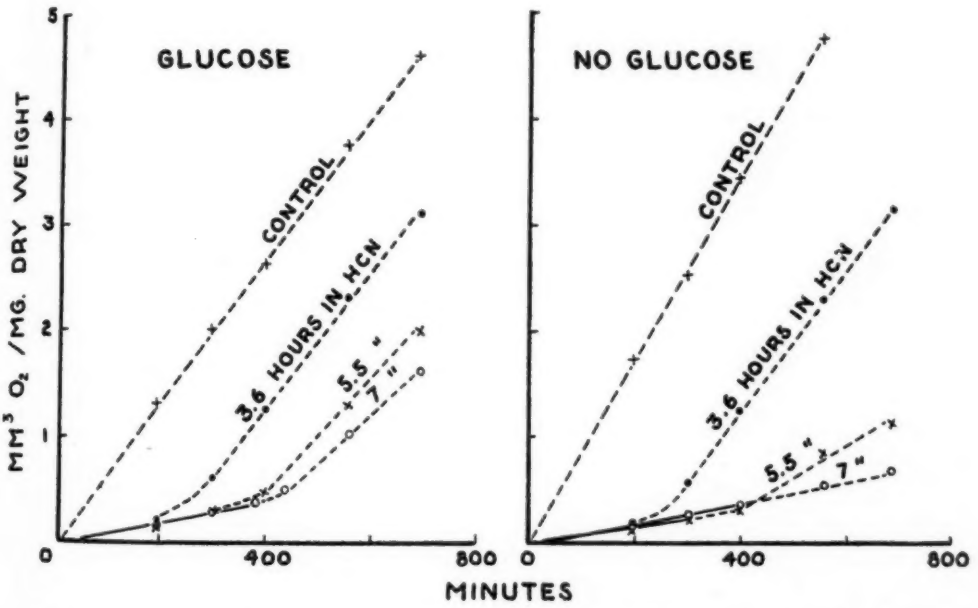

Fig. 4 (Robbie, *et al.*). Recovery of corneas after various exposures to 10^{-3} M. HCN. 0.2-percent glucose in buffered saline solution for first experiment; no glucose in fluid used in second experiment.

mum thickness which is permissible with most other tissues, but, since both the rate of respiration and the rate of diffusion of gas undoubtedly vary in the different structural components, it is not practicable to determine the limiting thickness on a theoretical basis. Fischer[6] has shown that the cornea normally uses oxygen directly from the air, and Lee and Hart[7] found little change in oxygen uptake when rat corneas were measured in pure oxygen rather than air, indicating that respiration is maximum in air. In the present series of experiments several determinations were made using oxygen as the gas phase, and the rate of metabolism was found to be about the same as in air. The fact that the corneas may be used without the disturbance in normal structure which occurs when a tissue is sliced makes them favorable for certain types of long-term experiments. An indication of the normality of the tissue is given by the course of the oxygen uptake curves as shown in the figures. The control corneas may run for as long as 12 hours without a decrease in the rate of respiration.

The oxygen consumption of the intact cornea is due to the respiration of the epithelial and endothelial layers and to the relatively inactive stroma. It is impossible to strip off the two soft layers without injuring them drastically, but it is possible to estimate the amount of respiration they contribute to the total by measuring the oxygen consumption of the whole cornea and that remaining after the epithelium and endothelium have been removed. Table 1 presents the results of a number of measurements on normal corneas and those which have had the two outer layers scraped off. The oxygen consumption of the stroma layer is one third that of the whole cornea. Since the weight of this portion is about 15 times that of the remaining layers it is apparent that its rate of metabolism is actually very low. The calculated value for the Q_{O_2} of the combined epithelium and endothelium is of the same order as that for other soft tissues such as liver, but the rate of respiration of the stroma is only one fortieth this amount. Since the stroma layer is primarily structural in function, a low level of oxygen consumption is probably sufficient to take care of its metabolic requirements. The functionally more active epithelium is ordinarily in close contact with air and direct diffusion can provide sufficient oxygen. Previous investigators who have measured the respiration of the rabbit cornea have reported somewhat higher values for the Q_{O_2} than that shown in Table 1. Kohra[8] lists a figure of -1.56, and Orzalesi[9] gives -2.09 for the Q_{O_2} values.

TABLE 1

OXYGEN CONSUMPTION OF INTACT CORNEA, CORNEA WITH EPITHELIUM AND ENDOTHELIUM REMOVED BY SCRAPING, AND ESTIMATED VALUE FOR EPITHELIUM

Tissue	Number of Determinations	Mean Q_{O_2}	Range
		(MM^3O_2/Mg. Dry Weight/hour)	
Entire cornea	18	0.46	0.30–0.63
Stroma	22	0.15	0.07–0.25
Epithelium (estimated)	—	6 to 8	—

The scraped corneas are inhibited by cyanide to about the same extent as the intact ones, and 10^{-3} M. HCN produces

almost complete inhibition of respiration.

Living cells require continuous expenditure of energy for maintenance purposes. If this energy supply is blocked for a certain critical period, the cell dies. Most mammalian tissues may utilize carbohydrate by either aerobic respiration or glycolysis, and the cornea is apparently no exception. When atmospheric oxygen is available, most of the glucose substrate is metabolized to carbon dioxide and water. Under anaerobic conditions, possibly also when the eyes are closed and the oxygen tension is considerably reduced, the glucose breakdown proceeds only as far as lactic acid. Cyanide treatment produces the same result, because the normal oxidative pathway is blocked by cytochrome-oxidase inhibition. In either of these cases, the energy for survival may come from the glycolytic process and the cornea survives. With cyanide exposure, the glycolysis rate is increased because of inhibition of the Pasteur mechanism; the rate of corneal glycolysis in bicarbonate buffer is doubled by 10^{-3} M. HCN.

Figure 4 illustrates an experiment in which corneas were inhibited by cyanide for various periods and the recovery then observed. Although the respiration was depressed by the cyanide to 10 percent of the normal level for as long as seven hours, it came back immediately to the original level if glucose was present as substrate. The corneal cells apparently obtained their maintenance-energy requirements by glycolysis. The situation was quite different with those corneas that did not have added glucose as substrate. There was no recovery from a 7-hour exposure to cyanide even if glucose was added at the end of the period of inhibition. In this case the energy supply was probably interrupted at both the respiratory and glycolytic levels, the former by the cyanide and the latter by lack of substrate. The deprived cells simply exceeded the tolerance limit for energy deprivation and were irreversibly affected.

Control corneas with no added glucose will respire uniformly for at least 12 hours at a rate which is the same or higher than those supplied with substrate. This respiration is almost completely inhibited by cyanide, indicating that it is probably due to carbohydrate oxidation. Since no glucose has been added, the cornea itself must contain the source material. It is quite possible that the mucoprotein which contains carbohydrate and comprises about 4 percent of the cornea[10] is an adequate source for normal respiration for a long period. However, more than 10 times as much glucose must be converted by glycolysis to lactic acid to produce energy equivalent to that released when the substrate is completely oxidized. A source that might be adequate for respiration may soon be used up if the tissue depends only upon glycolysis for its energy. This rapid depletion of the carbohydrate reserve may depress the glycolytic process, and after seven hours in cyanide, as shown in Figure 4, the tissue can no longer recover. A comparable situation has been reported for brain tissue.[11] After exposure without substrate to anaerobic conditions there was an irreversible loss of glycolytic capacity due to nonregeneration of adenosine triphosphate.

Summary

The respiration of the cornea is almost completely inhibited by 10^{-3} M. HCN, indicating that most of the oxygen consumption is probably mediated by a cytochrome-cytochrome oxidase system. A 10^{-4} M. cyanide produces about 50-percent inhibition. Recovery from cyanide exposure is rapid, and it is necessary to maintain a constant tension of HCN gas in the manometer flasks by the use of a properly balanced alkali-cyanide center-

well absorbing solution.

Most of the oxygen consumption of the intact cornea is due to the epithelial layer. The Q_{O_2} of this portion is about -6 to -8, comparable to other soft tissue such as liver. The stroma which has been denuded of epithelium and endothelium by scraping has a very low rate, a Q_{O_2} of -0.15.

Corneas may be 90 percent inhibited by cyanide for seven hours or longer and will recover quickly and completely upon removal of the cyanide, if glucose is present in the suspension fluid. If the fluid contains no substrate, there is no recovery after this exposure period.

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Discussion

Dr. V. Everett Kinsey (Boston, Massachusetts): I would like to propose an alternative explanation to account for the increased effect of cyanide poisoning in the absence of glucose. I think, in general, the reversible poisons like HCN act by virtue of their ability to complete favorably for their substrate, in this case the substrate being cytochrome oxidase. Therefore, when you have glucose present, a certain number of molecules of glucol, if you like, combined with its substrate, the cytochrome oxidase, and when you have cyanide present, you have the competition of cyanide and glucose for the cytochrome oxidase.

I cannot cite the experiments, but I think there is a good deal of evidence in the literature that that is a mechanism which is fairly common, and I believe it will account for your results equally well with the one which you propose.

Dr. W. A. Robbie (Iowa City, Iowa): There is another type of experiment which has been performed that expresses in chemical language what I have said from the cellular standpoint. Some workers on brain metabolism found that in the absence of glucose, the glycolytic process, the ability to carry on glycolysis, was lost after a few hours. They found that this was due to the disappearance of adenosine triphosphate (ATP), and that the reaction was irreversible. After the tissue had gone for a certain length of time without any substrate, it was unable to produce this high-energy phosphate-bond linkage, which apparently is necessary for survival. Perhaps that is saying the same thing that I said in more chemical terms.

VISUAL EFFECTS OF TRIDIONE*

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A new synthetic compound, Tridione (3, 5, 5-trimethyloxazolidine-2,-4 dione, Abbott) has recently been used as an anticonvulsant in the treatment of epilepsy. A number of papers[1] describing the results obtained with this new drug mention the fact that patients frequently complain of visual symptoms associated primarily with high illumination. Such symptoms are reported by a majority of adults and adolescents, occasionally by younger children. The only paper devoted specifically to the discussion of the visual phenomena is a brief note by Vail,[2] who reports that some patients experience difficulty in discriminating black or colors against light backgrounds and that visual acuity, although normal in low illuminations, may decrease to about 20/100 when the chart is illuminated to the customary level. It is reported that no external or ophthalmoscopic changes were found to account for these abnormalities in visual function.

The purpose of this paper is to report the results of a series of tests of visual function which provide further information as to the nature of the unusual visual phenomena associated with Tridione therapy. In preliminary studies, attempts were made to measure visual acuities for a wide range of illuminations including the high levels normally occurring outdoors. It was found that the previous state of adaptation of the eye and also its time of exposure to the brightness level at which acuity is measured are very important factors and must be carefully controlled if reproducible measurements are to be obtained. Marked reduction in acuity can, for example, be demonstrated immediately after change in the illumination from a moderate to a high level and vice versa, in patients showing little or no impairment of acuity after exposure for 10 minutes or more to the brightness level at which acuity is measured. Therefore, in the experimental procedures finally adopted, tests of visual function were made primarily at two brightness levels, 2 millilamberts and 2,000 millilamberts, and emphasis was placed on measurements of the rate of recovery of visual function with continued exposure to each brightness level. Tests of both visual acuity and differential brightness sensitivity at the fovea were used in the experiments. Supplementary studies included determinations of the light threshold, tests of color discrimination at high intensity, and tests of sensitivity to flicker.

The subjects were seven patients from the Baltimore City Hospitals, one aged 30 years, the others between 56 and 68 years of age. Those with uncorrected vision of 20/30 or better did not wear glasses during these tests. All tests were made with the natural pupil. In most experiments only one eye was tested. Comparison of the results of monocular and binocular tests of acuity in two patients showed the results to be essentially similar. The dosage of Tridione was 1 gm. per day in six cases, 3 gm. per day in one case, that of R. DeC. The patients were studied while on Tridione for periods varying from two to nine months. Recovery from the visual changes after discontinuance of the drug was studied in three cases.

* Read at the 16th scientific meeting of the Association for Research in Ophthalmology, Inc., Atlantic City, June 10, 1947. From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital and the Baltimore City Hospitals.

The authors are indebted to Miss Lorraine Wollach for assistance in giving the tests employed in this study.

I. Visual acuity

1. Apparatus

Visual acuity was tested with a special series of charts composed of Landolt rings which, at a distance of five meters, corresponded to acuities of 0.1, 0.15, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.25, 1.50, and 1.75. In each size four positions of the break in the ring—up, down, right, and left—were used. The smallest size at which the patient could read correctly at least three of the four figures was taken as the measure of his acuity. Each group of figures was mounted on a piece of white cardboard, five inches in width,

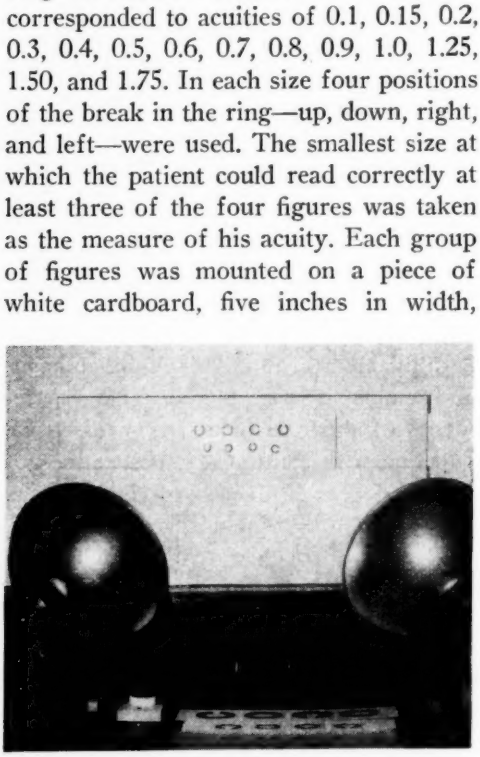

Fig. 1 (Sloan and Gilger). Arrangement of equipment for testing visual acuity.

which could be slipped into guides at the center of a white cardboard screen. At five meters this screen subtended a visual angle of 11.5 degrees in the horizontal and 5.8 degrees in the vertical dimension (fig. 1). With these charts it is possible to make repeated rapid measurements of acuity without any possibility of memorizing by the patient. High intensities of illumination were obtained by means of two 500-watt photoflood lamps enclosed in bowl-shaped reflectors. The distance of these from the screen was adjusted to give an even illumination of the desired amount. Lower intensities of illumination were provided by ordinary incandescent lamps in ceiling fixtures. A Macbeth Illuminometer was used to measure the brightness of the white background of the test charts.

2. Results

A. Recovery of visual acuity at 2,000 millilamberts after adaptation to 2 millilamberts. In these tests the eye was first exposed for 10 minutes to the white screen illuminated to a brightness of 2 millilamberts. The illumination was then increased to give a brightness of 2,000 millilamberts, and measurements were made immediately and as rapidly as possible thereafter until acuity reached a constant level. When the increase in acuity was relatively slow it was possible to obtain very accurate measurements of the time required to reach each successive level of acuity. When recovery was rapid the successive stages could be measured only approximately.

The results of such tests are shown in Figures 2 to 5. In these graphs the times of exposure to 2,000 millilamberts are plotted on the abscissa, the corresponding acuities in logarithmic units on the ordinate. A logarithmic scale of acuities is used, rather than a linear scale, because it minimizes on the graph the unavoidable fluctuations in acuity which occur as the maximal level is approached.

In order to obtain comparative data on the normal rate of recovery of acuity, this test was given to four of the patients prior to Tridione therapy. While there may be, in normal subjects, a momentary reduction in acuity with sudden change in brightness from 2 to 2,000 ml., the time required to reach maximum acuity was less than one minute in every case and therefore could not be measured accurately by the procedures used in this study. Craik,[3] using more accurate methods of measurement, found no significant reduc-

tion when acuity was measured within two seconds after change in brightness from about 1 to 1,000 ml.

The patients on Tridione, however, all showed a significant reduction in acuity immediately after exposure to the high brightness. Figure 2 gives typical recovery curves for each of the seven patients. In five cases the acuities were 20/200 or less after only one minute of exposure to the high brightness. With longer exposure, the acuity increased gradually, then reached a constant level. For most subjects this final level was equal to or better than that at 2 ml. Impairment of acuity is, therefore, only temporary and after sufficient time of exposure to the high brightness there is no measurable defect. The recovery curves of two patients, W. C. and G. T., however, revealed a marked reduction in acuity even after adaptation for 10 or more minutes to the high brightness. The course of the recovery curves indicates that in these patients there was lasting impairment of acuity at the high brightness level, demonstrable even after long-continued exposure.

The rate and extent of recovery of acuity varied with duration of therapy. Five patients were tested at intervals while taking Tridione for periods of time varying from 7 to 28 weeks. Progressive changes in the recovery curves of three

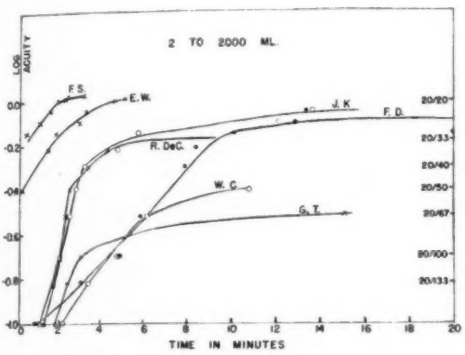

Fig. 2 (Sloan and Gilger). Rate of recovery of acuity after change from 2 to 2,000 ml. Typical curves for each patient. In normal subjects recovery is practically instantaneous.

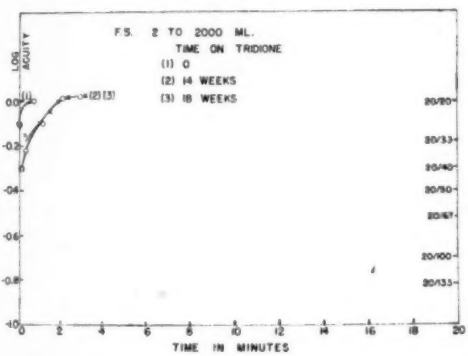

Fig. 3 (Sloan and Gilger). Change in rate of recovery of acuity with duration of therapy. Subject F. S.

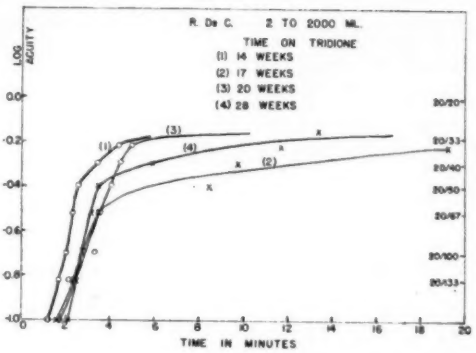

Fig. 4 (Sloan and Gilger). Change in rate of recovery of acuity with duration of therapy. Subject R. DeC.

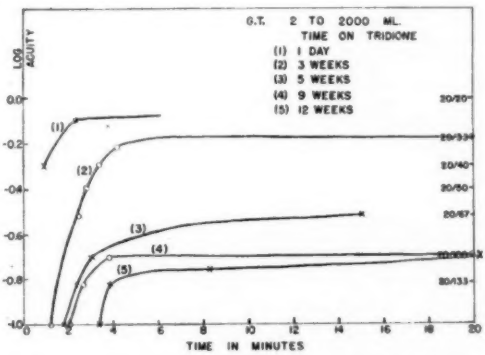

Fig. 5 (Sloan and Gilger). Change in rate of recovery of acuity with duration of therapy. Subject G. T.

patients illustrating different degrees of defect are shown in Figures 3 to 5. F. S. showed only a slight impairment of essentially the same degree after 14 and 18 weeks of therapy. For R. DeC., the rate of recovery was slower after 17 than after 14 weeks. The curves for 20 and 28

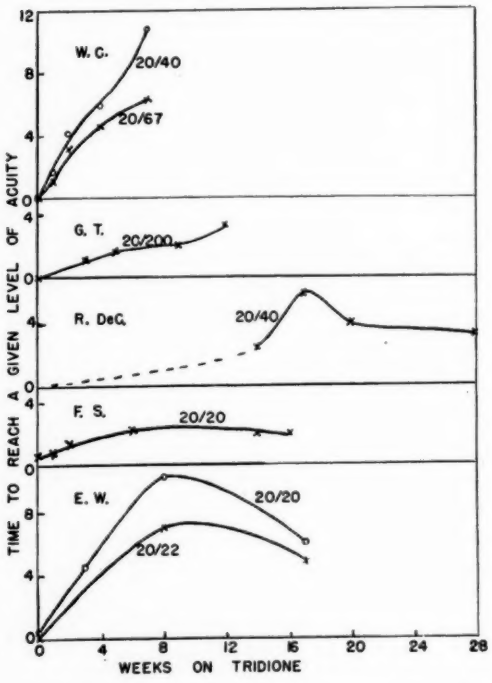

Fig. 6 (Sloan and Gilger). Changes in rate of recovery of acuity at 2,000 ml. with duration of therapy. The time required to attain a given acuity is taken as an index of rate of recovery.

weeks of therapy, however, showed no further progressive impairment and in fact some evidence of improvement. G. T., followed for only 12 weeks on Tridione, showed marked impairment increasing in severity with duration of therapy.

The relationship between delay in recovery of acuity and duration of therapy is also shown in Figure 6. This chart gives the time required to reach a given level of acuity. The acuities chosen in each case are indicated on the individual curves. It is apparent from these curves that for all five patients there was a gradual slowing in rate of recovery during the first seven weeks. The results for those followed for 14 weeks or more indicate that after long-continued therapy the recovery curves become approximately constant or show slight improvement, suggesting that the patients gradually developed a tolerance to the visual effects of the drug. It is of importance to determine in future studies whether patients with marked defects, such as were manifested by our subjects, W. C. and G. T.,

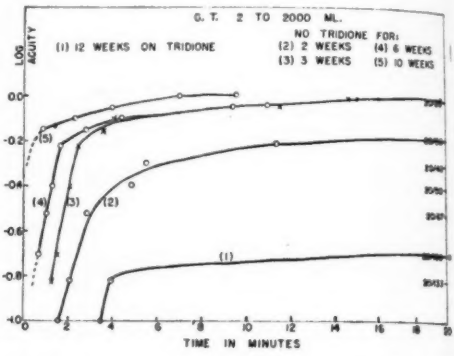

Fig. 7 (Sloan and Gilger). Improvement in recovery curves of acuity at 2,000 ml. when Tridione was discontinued. Subject G. T.

also reach a constant level of impairment after long periods on Tridione.

Three patients, G. T., F. D., and J. K., whose recovery curves were measured 8 or 10 weeks after Tridione was discontinued, all had approximately normal rates of recovery at this time. Figure 7 shows for G. T. the gradual restoration to normal during a period of 10 weeks.

B. Recovery of acuity at 2 millilamberts after adaptation to 2,000 millilamberts. The results reported in the previous section indicated that Tridione produces a delay in the rate of light adaptation, as measured by tests of visual acuity. It might be expected, therefore, that the reverse change from high to low brightness would also produce a similar temporary

impairment of visual acuity. Studies were therefore made to test this assumption.

With change from 2,000 to 2 ml., normal subjects and patients tested prior to Tridione therapy reached a maximum acuity in less than one minute. A typical recovery curve for each of the six patients given this test is shown in Figure 8. The individual differences in rate of recovery correspond closely to those of the previous test. As before, F. S. and E. W. showed the most rapid rates, G. T. and W. C. the slowest. Adaptation of one eye to the high brightness did not produce any impairment in the unexposed eye when the latter was tested at 2 ml.

Recovery of acuity with change from high to low brightness differs in one important respect from that observed with change from low to high brightness. The final level of acuity at 2 ml., reached after continued exposure to this brightness, was in no case lower than the acuity prior

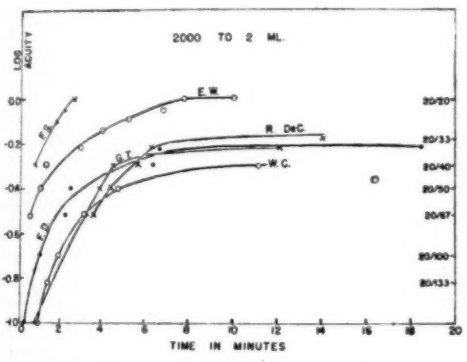

Fig. 8 (Sloan and Gilger). Rate of recovery of acuity after change from 2,000 to 2 ml. Typical curves for each patient. In normal subjects recovery is practically instantaneous.

to therapy. There is, therefore, no evidence of lasting impairment at the low brightness such as was observed in several patients at 2,000 ml.

C. Variation of acuity with intensity. It was shown in the previous sections that after adequate time of adaptation to the brightness at which acuity was measured all subjects had normal acuity at 2 ml., while some showed significant impairment at 2,000 ml. Measurements of acuity at intensities between 2 and 2,000 ml.

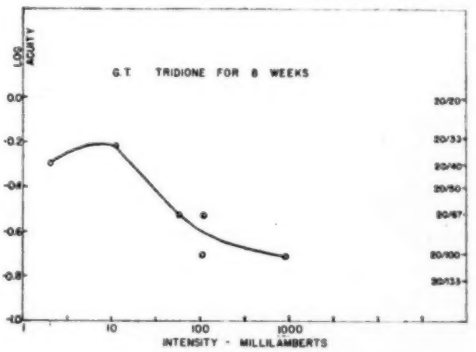

Fig. 9 (Sloan and Gilger). Variation of acuity with light intensity. Subject G. T. In these tests the eye was adapted to each brightness before acuity was measured.

were made for G. T., one of the patients showing markedly reduced acuity at 2,000 ml. The tests at each intensity were continued until there was no further improvement in order to insure that maximal acuity was reached. The results are shown in Figure 9. Brightness in log units is plotted on the horizontal coördinate, acuity in log units on the vertical. At 10 ml., the acuity of 20/33 was equal to that prior to therapy. At 50 ml., it decreased to 20/70; at 1,000 ml., to 20/100. The fact that this patient complained of impaired vision only in outdoor illuminations is consistent with these findings, since indoor brightnesses are seldom greater than about 30 ml.

II. Differential brightness sensitivity

1. Apparatus

The test for brightness discrimination employed gray strips (1° by 0.5°), mounted on a white background. The percent contrast depends upon the reflect-

ances of the strip and the background and is given by the formula: percent contrast equals $100(R_b - R_s)/R_b$ where R_b is the reflectance of the white background (0.88) and R_s that of the strip (0.80 to 0.024). The eight steps of contrast are

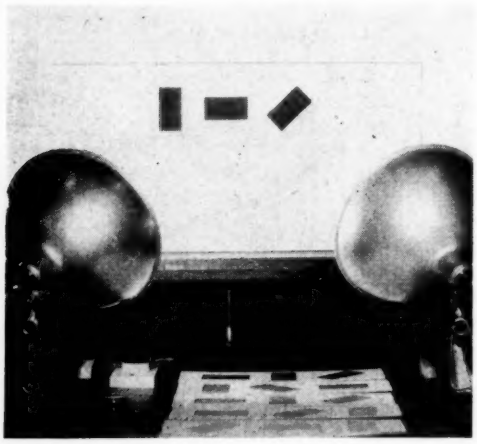

Fig. 10 (Sloan and Gilger). Arrangement of equipment for testing contrast (differential brightness) sensitivity.

9.1, 30.3, 50.0, 64.1, 76.5, 88.1, 95.4, and 97.5 percent. Three strips in different orientations were used at each contrast level. The patient was required to report whether the orientation of each strip was horizontal, vertical, or diagonal. The minimum perceptible contrast is taken as that at which the position of all three strips was named correctly. As in the acuity tests, the charts were shown at the center of the large white cardboard screen (fig. 10). The provisions for illumination of the chart and surrounding area were the same as those employed in the tests of visual acuity.

The minimum contrast perceptible by the normal eye is about two percent at high-brightness levels. In these studies no attempt was made to provide contrasts smaller than 9 percent because of the difficulties in measuring and standardizing smaller differences in reflectance. For this reason and because the contrast steps are relatively large, this test equipment is suitable only for the measurement of relatively gross changes in contrast sensitivity.

2. Results

A. Recovery of differential brightness sensitivity at 2,000 millilamberts after adaptation to 2 millilamberts. Four patients tested prior to Tridione therapy were all able to perceive the smallest contrast step (9 percent) within six seconds after a sudden change from low to high brightness. Figure 11 gives typical recovery curves for each of the six patients given this test while on Tridione. The two showing the most rapid recovery, F. S. and E. W., required more than three minutes of exposure to the high brightness before they were able to perceive the 9-percent contrast. Three patients with slower rates of recovery, F. D., R. DeC., and G. T., required from four to five minutes to detect the 30-percent contrast. The slowest rate of recovery was shown by W. C., who required about eight minutes to see the 30-percent contrast and

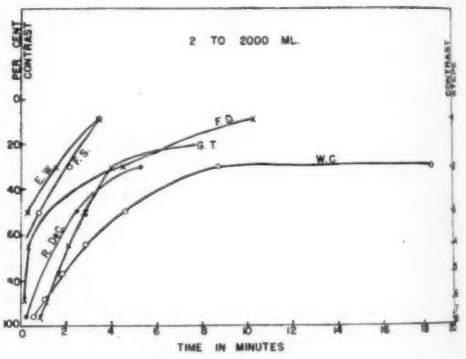

Fig. 11 (Sloan and Gilger). Recovery of contrast sensitivity after change from 2 to 2,000 ml. Typical curves for each patient. In normal subjects recovery is practically instantaneous.

could not get the next step (9 percent), after an exposure of 18 minutes to the high brightness. Figure 12 shows changes

in the recovery curves with time on Tridione for G. T., one of the patients with a relatively slow rate of recovery. After 12 weeks he was unable to distinguish a strip 50-percent darker than the background even after long exposure to the high brightness. Recovery of contrast sensitivity after the drug was discontinued is shown in Figure 13. In spite of the marked impairment after 12 weeks on Tridione, the results were approximately normal six weeks after it was discontinued.

B. Recovery of differential brightness sensitivity at 2 millilamberts after adaptation to 2,000 millilamberts. Three patients, were given this test prior to Tridione

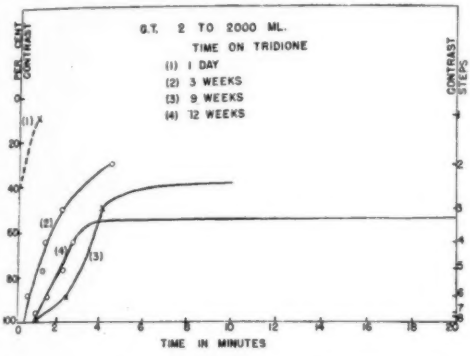

Fig. 12 (Sloan and Gilger). Changes in rate of recovery of contrast sensitivity with duration of therapy. Subject G. T.

therapy. The time required to perceive the 9-percent contrast was less than 0.3 minutes in every case. Five patients were tested at intervals while taking Tridione. Recovery curves for W. C. are shown in Figure 12 to illustrate typical results. It may be seen that while there was a significant retardation in recovery, the rates were too rapid in this test to permit an accurate determination of the course of the curves. The times required by W. C. to perceive the 9-percent contrast varied from 1.5 minutes to 2.4 minutes in the different tests. The maximum times re-

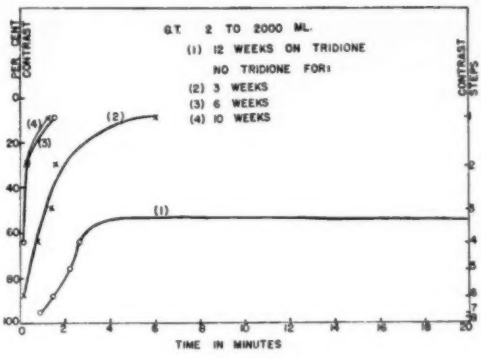

Fig. 13 (Sloan and Gilger). Improvement in recovery curves of contrast sensitivity when Tridione was discontinued. Subject G. T.

quired by each of the five patients to reach this point on the curve are listed in Figure 14. F. S. and E. W., as in previous tests, showed the least deviation from normal and required only 0.5 and 1.1 minutes, respectively, to perceive the 9-percent contrast. These times, although short, probably represent a true impairment, since prior to therapy both patients required less than 0.1 minute.

Individual differences in the rate of recovery of brightness discrimination,

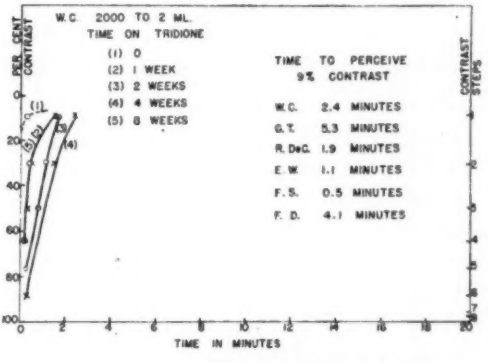

Fig. 14 (Sloan and Gilger). Rate of recovery of contrast sensitivity after change from 2,000 to 2 ml. The curves on the left show changes in rate of recovery for one patient, W. C., with duration of therapy. The tabulated data on the right give the maximum times required by different patients to perceive a 9-percent contrast. In normal subjects recovery is practically instantaneous.

with change from high to low brightness and the reverse, correspond closely to the individual differences in rate of recovery of visual acuity. The more rapid recovery of contrast sensitivity than of acuity may be attributed in part to the fact that the smallest contrast measured is greater than the minimum which can be perceived by the normal subject. Because of this, recovery of contrast sensitivity could not be followed to its maximum.

The general similarity in the results of the two types of test suggests that poor brightness discrimination rather than impaired resolving power of the retina is the primary factor responsible for the reduction in visual acuity. This is supported by the statements of the patients that they could not see the test letters immediately after increase in the illumination because everything looked white.

III. Tests of the light threshold

The instrument and procedure used in these studies has been described in detail elsewhere.[4]

1. Threshold of the dark-adapted eye

The thresholds of the fully dark-adapted eye were measured at 19 different locations in the horizontal meridian, extending from the fovea to the far periphery both nasally and temporally. The average of these 19 thresholds, designated hereafter as the "horizontal-meridian threshold" provides a sensitive index of changes in the general level of sensitivity of the rod mechanism throughout the retina.

Three patients, E. W., F. D., and W. C. were tested before and during Tridione therapy. The horizontal-meridian threshold of E. W. before therapy was 5.32 (log micromicrolamberts); after three weeks on the drug, 5.10; after 16 weeks, 5.0. The thresholds of F. D., in four successive tests during a period of four months prior to therapy, were 5.30, 5.22, 5.13 and 5.22; after eight weeks on Tridione, the threshold was 5.29. In these two patients the evidence is unequivocal in showing no significant increase in rod thresholds at a time when tests of visual acuity and brightness discrimination revealed marked impairment of cone function. The data for the third patient, W. C., are less satisfactory because of the greater variability in successive tests. The horizontal-meridian threshold prior to therapy was 5.43; after one week on the drug, 5.73; after two weeks, 4.92. Tests of acuity and brightness discrimination showed greater impairment of cone function after two weeks than after one week of therapy; whereas, the increase of 0.3 log unit in the rod threshold after one week was not confirmed in the test made after two weeks. It may be concluded, therefore, that in this case also, Tridione had no measurable effect on the rod thresholds of the dark-adapted eye.*

2. Rate of dark adaptation

Tests of differential brightness discrimination, it will be remembered, showed a slight delay in rate of recovery of sensitivity at 2 ml. after adaptation to 2,000 ml. A similar delay in rate of recovery of sensitivity of the cones or the rods or of both, might therefore be expected when the brightness threshold in-

* The horizontal-meridian thresholds of these patients are all close to the upper limit of normal. The thresholds of normal individuals, corrected for size of pupil, range from 3.8 to 5.1. Without pupil correction a somewhat greater range is to be expected. It was impossible in this study to make such corrections because photoflash bulbs for photographing the pupil could not be obtained. It is possible, therefore, that small pupils account for the relatively high thresholds. Although the patients were on institution diets perhaps low in vitamin A, this factor can be ruled out in the case of F. D., since after the first light-sense test he received daily supplements of vitamin A during the entire period of the tests.

stead of the just noticeable difference in brightness is used as a measure of sensitivity.

The rate of dark adaptation at the fovea was determined for one patient, E. W., before and during Tridione. The results are shown in Figure 15. The increase in light thresholds after 3 and 16 weeks on Tridione is slight and perhaps not significant in view of the normal day to day variation in threshold measurements. It is, however, of about the magnitude that would be expected from the results of the tests of differential sensitivity for this patient. Before therapy the time required to perceive a 9-percent contrast at 2 ml. after adaptation to 2,000 ml. was less than 0.1 minute; after 10 weeks on Tridione, it was 1.1 minute. It may be seen from Figure 15 that the light threshold reached in 0.6 minute prior to therapy is reached in about 1.7 minute. The delay in reaching a given level of sensitivity is therefore about the same in the two tests.

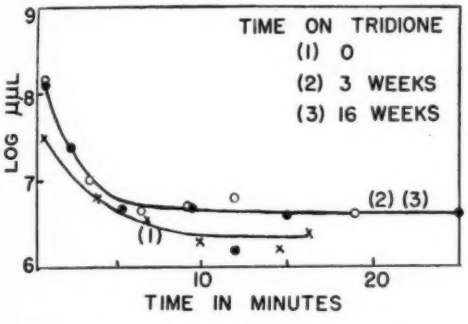

Fig. 15 (Sloan and Gilger). Rate of dark adaptation at the fovea after preadaptation to 1,100 ml. A 1-degree white test field was used. Subject E. W.

Similiar tests of the rate of dark adaptation, but at 15 degrees in the nasal field instead of at the fovea, were given to another patient, F. C. Four tests prior to Tridione and one test after 8½ weeks of therapy were made. The results are shown in Figure 16. This patient shows no significant change in cone adaptation since the curve obtained during therapy lies within the range of variation observed in the control tests. In the test of differential brightness sensitivity given on the same day, however, he required 4.2 minutes to detect a 9-percent difference in contrast. This difference in the results of the two tests may indicate a greater impairment of the foveal than of the parafoveal cones. The second section of the adaptation curves, which measures the rate of adaptation of the rods, likewise shows no significant change with Tridione. Here, however, the variation in the data obtained prior to therapy is as much as 0.9 log unit, so that in this patient slight changes in rate of adaptation of the rods could not have been detected.

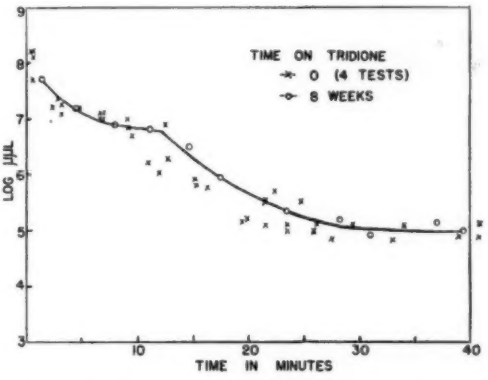

Fig. 16 (Sloan and Gilger). Rate of dark adaptation at 15 degrees in the nasal field after preadaptation to 1,100 ml. A 1-degree white test field was used. Subject F. D.

Tests of the light threshold, therefore, did not reveal any marked impairment of cones or rods, either during adaptation to darkness or after dark adaptation was complete. It is possible that the rods may show impaired function at higher intensities, such as was demonstrated in the case of the cones by other tests. Since there are no retinal areas containing rods

alone, practical difficulties arise in completely separating rod and cone function at intensities well above the rod threshold. Determinations of the variation in brightness or flicker sensitivity with variation in intensity in the scotopic range, if made before and after Tridione therapy, might however provide an answer to this problem. It is planned to make such tests in future studies.

IV. Color discrimination

1. General observations

The Ishihara Pseudo-isochromatic Plates, viewed in an illumination of about 20 foot-candles, were read correctly by all patients. This finding ruled out congenital red-green color deficiency and was consistent with the results of other tests showing that color discrimination is impaired only at high intensities. The visual fields for 1-degree blue and red test objects were normal when determined under standard conditions with a Brombach perimeter. When, however, a white background was substituted for the black perimeter arc and the illumination was increased from the standard value of 10 foot-candles to about 200 foot-candles, 1-degree blue and red test objects were recognized only at the fixation point. Under these experimental conditions, normal controls do not show any similar contraction of the color fields. This finding indicates that visual impairment is not limited to the foveal cones, and probably involves cone function throughout the entire retina. Further evidence of anomalous color perception is the erythropsia at high illuminations reported in the early stages of therapy by three patients. During the tests of brightness discrimination, one patient volunteered the information that the gray strips on the white background and other darker areas in the field of view appeared pink.

2. Special test of color vision

Additional information as to the nature of the distortions of color perception was obtained from a special test of color discrimination similar to that used to measure brightness discrimination.

A. Apparatus. The equipment may be described briefly as follows: oblong strips (1° by ½°) of red, green, blue, and yellow are shown on backgrounds of approximately the same reflectance as the strip. Each background is a 1.6-degree square, either gray or a chromatic color differing from the test strip. The strips on their respective backgrounds are shown two at a time in an aperture in a white screen illuminated to a brightness of 2,000 ml. The brightnesses of the colors are somewhat less, the exact values depending on their reflectances. The test strips and their backgrounds were selected from standard Munsell pigment papers. In each of the four hues, strips of low, moderate, and high chroma (saturation) are used. The Munsell specifications for the 24 combinations of strip and background are listed in Table 1. These define the colors of the papers when illuminated by light of daylight quality. In illumination from photoflood lamps such as was used in most of our tests, there is probably a considerable decrease in chroma of the blues, and some increase in that of the reds.[5]

B. Results. In tests made prior to Tridione therapy, all the colored strips were identified correctly with the exception of green, which was occasionally called blue or geenish-blue particularly when on a yellow background. Of the five patients tested at a high illumination while on Tridione, all but one, F. S., showed significant abnormalities in color discrimination. The findings summarized in Table 1 illustrate the type and degree of impairment observed. The tests were given after 5 to 20 minutes' exposure to 2,000 ml. It

was not feasible to make accurate tests of changes in color discrimination with time of exposure to the high brightness because of the length of time required to present all the color combinations. It was, nevertheless, apparent that color discrimination improved somewhat with continued exposure. The results in Table 1 represent the most marked defects observed in each patient.

TABLE 1

COLOR DISCRIMINATION IN HIGH ILLUMINATION

Group	Munsell Specifications*		Color of Strip Seen by Patients†			
	Strip	Background	G. T.	R. DeC.	F. D.	E. W.
I	R 5/12	N 5/	Yellow	Yellow	Yellow	Yellow
	R 6/6	N 6/	0	Yellow	White, later yellow	Yellow
	R 6/4	N 6/	0	Yellow	White	Yellow
	R 5/12	Y 5/6	Yellow	Yellow	Yellow	+
	R 6/6	Y 6/6	0	White	O, later white	+
	R 6/4	Y 6/4	0	White	O, later white	+
II	G 5/8	N 5/	0	+	+	+
	G 6/6	N 6/	0	+	White	+
	G 6/4	N 6/	Blue	+	White	+
	G 5/8	Y 5/6	Blue	Blue	+	+
	G 6/6	Y 6/6	White	Blue	Blue, later gray	Blue
	G 6/4	Y 6/4	White	Blue	White, later gray	Blue
	G 6/6	R 6/6	0	+	+	+
	G 6/4	R 6/4	0	+	Yellow, later gray	+
III	PB 3/12	N 3/	+	+	+	+
	PB 6/6	N 6/	0	+	White	+
	PB 6/4	N 6/	0	+	White	+
	PB 6/6	Y 6/4	White	+	White	+
	PB 6/4	Y 6/4	White	+	White	+
	PB 6/6	G 6/6	White	+	White	+
	PB 6/4	G 6/4	0	+	White	+
IV	Y 8/12	N 8/	+	+	+	+
	Y 6/6	N 6/	+	+	+	+
	Y 6/4	N 6/	+	+	+	+

* The numerator of the fraction specifies the Value (a measure of lightness). The denominator specifies the Chroma (saturation). N indicates a neutral color, that is, a gray. Neutral colors are of zero Chroma.

† + indicates a correct response; 0 indicates that no strip was seen.

In Group I, composed of red strips on gray or yellow backgrounds, the strip was sometimes not seen at all, indicating that it was a close match to the background. In other cases the strip was reported as yellow, white, or gray. In Group II, green strips on various backgrounds, the strips were usually reported as blue, gray, or white. Calling the green strip blue may not be of significance since this error was also made prior to therapy. In Group III, the most saturated blue (chroma 12) was always identified correctly. Blues of lower chroma were reported as white by two patients. In Group IV, yellow strips on gray backgrounds, none of the patients made any errors. In the yellowish illumination from the photoflood lamps, yellows are of higher saturation than blues of the same nominal chroma. For this reason it cannot be definitely concluded from these findings that there is a greater impairment of sensitivity to blue than to yellow, The findings do suggest, however, that

perception of red and green is more impaired than perception of blue and yellow.

V. Flicker sensitivity

Tests of sensitivity to flicker, while not directly related to the visual discriminations required in the ordinary use of the eyes, may nevertheless be of aid in explaining the visual impairment produced by Tridione. The critical flicker frequency, or rate of alternation of dark and

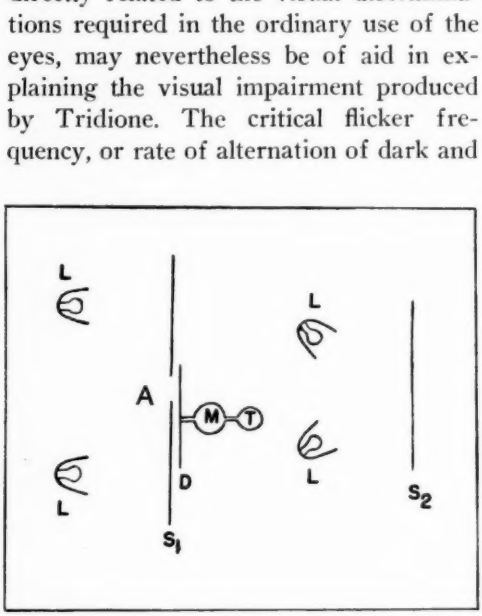

Fig. 17 (Sloan and Gilger). Arrangement of equipment for measuring critical frequency of flicker. S_1, illuminated surround. A, 1-degree square aperture through which subject views illuminated screens, S_2. D, sectored disc. M, motor. T, tachometer. L, lamps in reflectors.

light flashes at which the sensation of flicker disappears, has been extensively investigated under a number of experimental conditions. Such studies have been made not only in man, but also in many of the lower animals which respond with characteristic reflex movements to a flickering light. It is possible that a final explanation of the effects of Tridione on the visual mechanism may require parallel experiments on animal subjects. Since measurements of critical flicker frequency in human beings can more easily be duplicated in animal experiments than can measurements of acuity or brightness discrimination, they may contribute both directly and indirectly to our knowledge of the effects of Tridione on vision.

1. Apparatus for measuring critical frequency of flicker

The arrangement of apparatus is shown diagrammatically in Figure 17. S_1 and S_2 are white screens, reflectance 0.88, which may be illuminated to any desired brightnesses. The square aperture, A, through which the observer views S_2, serves as the test field; the square field, S_1, as the surround. The test field and surround subtend visual angles of 1 degree and 10 degrees, respectively. A rotating, sectored disc, D, is located directly behind aperture, A. The closed sectors of the disc are painted a matt black (reflectance 0.06).

This apparatus differs in two ways from that usually employed[6] in measuring critical flicker frequency (c.f.f.) in man. First, the illumination of the test field is not cut off simultaneously over its entire area. Second, the light illuminating the surround also falls on the black sectored disc. In Series A, in which the surround is matched to the test field at each intensity, the dark phase of the flickering light has a brightness about 3.5 percent of that of the light phase. In Series B and C, in which the surround is maintained at a constant low brightness of 1 ml., the dark phase is only 0.07 ml. The experimental conditions of this study are therefore somewhat similar to those frequently used in animal experiments in which moving black and white stripes provide the flicker stimulus.[7] The findings may perhaps differ slightly from those obtained when the entire flicker field is reduced simultaneously to zero brightness. Valid comparisons are nevertheless possible between the data for normal controls and those for patients on Tridione when both are tested under identical conditions.

2. Results

Series A. In the first series of experiments the c.f.f. in cycles per second was measured at fusion brightnesses of the test field ranging from about 1 to 1,000 ml. The flicker disc was composed of equal open and closed sectors. The fusion brightness of the test field was therefore one half the brightness of the illuminated screen S_2. The brightness of the surround, S_1, was matched in each case to the brightness of the test field at fusion.

Results are given in Figure 18 for four normals and three patients on Tridione. In normal subjects, the c.f.f. increased with increase in brightness of the test field up to about 300 ml. (2.5 log units), then became constant or decreased slightly. In the three patients on Tridione, the c.f.f. followed a normal course up to about

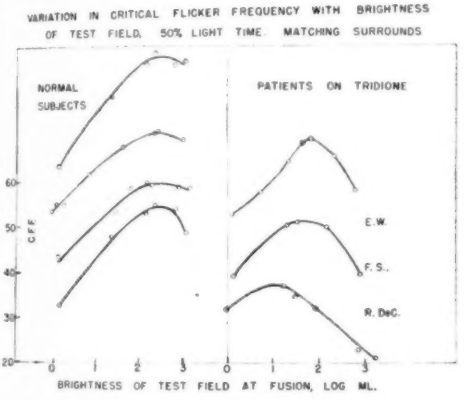
VARIATION IN CRITICAL FLICKER FREQUENCY WITH BRIGHTNESS OF TEST FIELD. 50% LIGHT TIME. MATCHING SURROUNDS
NORMAL SUBJECTS
PATIENTS ON TRIDIONE
E.W.
F.S.
R. DeC.
C.F.F.
BRIGHTNESS OF TEST FIELD AT FUSION, LOG ML.

Fig. 18 (Sloan and Gilger). Variation in c.f.f. with variation in fusion brightness of the test field when the surround is of the same brightness as the test field. The lowest curve in each group is in the correct location. The others are shifted upward in steps of 10 units on the vertical ordinate.

30 ml. (1.5 log units) then decreased at higher brightnesses.

The measurements of c.f.f. charted in Figure 18 are those obtained after adaptation to each brightness for the time necessary to reach a constant level of flicker sensitivity. It is of interest that, although marked impairment of sensitivity to flicker persisted after adaptation to high brightness, the visual acuity and

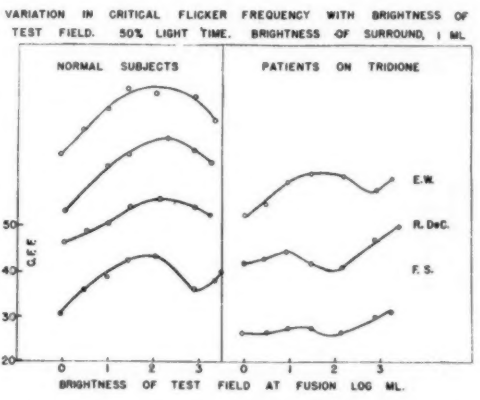
VARIATION IN CRITICAL FLICKER FREQUENCY WITH BRIGHTNESS OF TEST FIELD. 50% LIGHT TIME. BRIGHTNESS OF SURROUND, 1 ML.
NORMAL SUBJECTS
PATIENTS ON TRIDIONE
E.W.
R. DeC.
F.S.
C.F.F.
BRIGHTNESS OF TEST FIELD AT FUSION LOG ML.

Fig. 19 (Sloan and Gilger). Variation in c.f.f. with variation in fusion brightness of the test field when the brightness of the surround is 1 ml. The curves are separated vertically as in the previous figure.

differential brightness sensitivity of these three patients nevertheless showed complete recovery after adequate light adaptation. In one case, R. DeC., alternate measurements of acuity and c.f.f. were made at the same high brightness until both reached constant levels. This test proved conclusively that, under identical experimental conditions, visual acuity may be normal and sensitivity to flicker markedly reduced.

Series B. In the second series of flicker experiments the brightness of the surround was maintained at a constant low value of 1 ml. The other experimental conditions were the same as in Series A. Figure 19 gives the c.f.f.–Log-I curves for four controls and three patients on Tridione. The curves of normal subjects were in general similar to those obtained by them with matching surrounds, but showed slightly lower values of c.f.f. throughout, and a more marked drop at high intensities. These differences are in

accord with the results of previous investigations.[8]

The curves of the patients on Tridione, however, differed markedly from normal. Their irregular course suggests that two opposing factors were at work, one producing a decrease, the other an increase

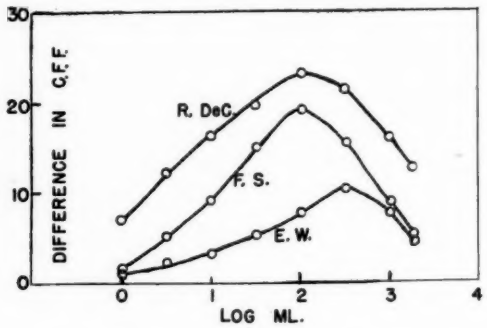

Fig. 20 (Sloan and Gilger). Difference between the values of c.f.f. for a normal subject and for each patient on Tridione. The data are obtained from the curves of Figure 19.

in c.f.f., with increase in intensity. This is more clearly evident in a graph showing, not the actual values of c.f.f. at each intensity, but the difference between these values and those of a normal subject. Such data are shown for each of the three patients in Figure 20. Impairment in flicker sensitivity, as indicated by the degree of deviation from the curve of a normal subject, increased regularly for all three patients with increase in intensity up to 2 or 2.5 log units. At still high intensities there was a gradual return toward normal. The data obtained with matching surrounds, on the contrary, showed gradually increasing impairment with increase in intensity and no evidence of recovery at high intensities. The difference in the results of the two tests is apparent in Figure 21 where both curves are shown on the same graph for one patient who was given the two tests on the same day. The most marked difference occurred at the highest intensity, 1,740 ml. (3.24 log units), where the c.f.f was 39.6 when determined with a low surround, but only 20.6 when determined with a matching surround. Additional experiments indicated that the effect of the different surrounds on the c.f.f. cannot be attributed to the difference in level of light adaptation. When the eye was adapted to 1 ml., and the surrounding field was suddenly increased to match the test field, the c.f.f. dropped immediately from 39.6 to 8.0, then rose gradually to 20.6 as the eye became adapted to the higher brightness. Conversely after adaptation to the higher brightness, with sudden decrease in the brightness of the surround to 1 ml., the c.f.f. rose immediately from 20.6 to 32.5, then showed a further rise to 39.6 as the eye became adapted to the lower brightness.

It appears, therefore, that the brightness of the surrounding field has an immediate and direct effect on sensitivity to flicker. Some process of facilitation may occur when the surround is much lower in brightness than the test field, and conversely a high brightness of surround may have an inhibitory effect on flicker discrimination. These effects, it will be

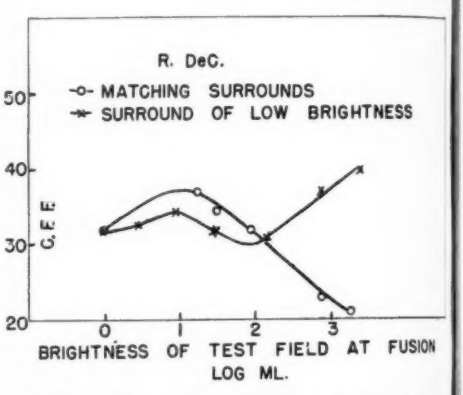

Fig. 21 (Sloan and Gilger). Comparison of the results when the brightness of the surround is maintained at a constant value of 1 ml., and when it matches the test field at each intensity. Subject R. DeC.

noted, are the reverse of those occurring in the normal eye. Such interaction between different retinal areas when manifested practically instantaneously cannot easily be explained in terms of photochemical changes and is, therefore, usually attributed to processes involving lateral connections in the neural layers of the retina.

Series C. In the two previous tests, the dark phase was 50 percent of the complete cycle. A third series of tests investigated the effect of variation in the relative lengths of the dark and light phases. Flicker discs with different sizes of closed sector provided dark-times of 10, 25, 50, 75 and 90 percent. Other experimental conditions were the same as in Series B.

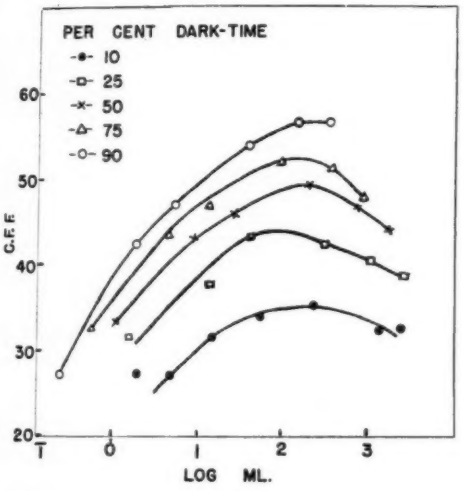

Fig. 22 (Sloan and Gilger). Variation in c.f.f. with variation in fusion brightness of test field for five different values of dark-time. Normal subject.

It has been shown in previous studies by Crozier, Ross, and others[9] that for constant brightness of the test field, the c.f.f. increases with increase in the dark-time. Our data, both for normal subjects and patients on Tridione, are in agreement with those of Ross, who found that fusion brightness and dark-time are independent variables whose effects on the critical frequency of flicker are additive. Data for a typical normal subject illustrating the effect on the c.f.f.–Log-I curve of change in dark-time are shown in

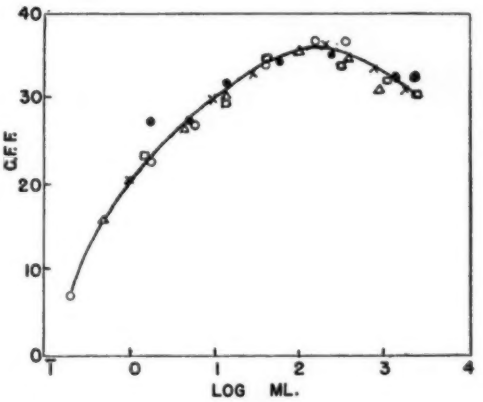

Fig. 23 (Sloan and Gilger). Replot of data of Figure 22 after applying corrections required to superimpose the data for five dark-times. The symbols have the same meaning as in Figure 22.

Figures 22 and 23. In Figure 22 it may be seen that the five curves for different dark-times follow approximately parallel courses, suggesting that increase in dark-time merely shifts the curve upward without changing its shape. In order to test this assumption the same data have been replotted in Figure 23 after applying suitably chosen corrections to compensate for the effect of increase in dark-time on the c.f.f. It may be seen from Figure 23 that it is possible to draw a single curve through the points representing the corrected values of c.f.f. for all five dark-times. The same treatment of the data of a second normal subject gave essentially similar results.

Similar tests were given to two patients on Tridione (figs. 24 and 25). Here, too, the data for different dark-times can be fitted approximately to single curve by subtracting a constant from the values of c.f.f. for each dark-time. The patients on Tridione, however, showed a smaller in-

crease in c.f.f. with increase in dark-time. Table 2 gives these data for the normal subjects and the patients on Tridione. For the two normals, the increase in c.f.f. with

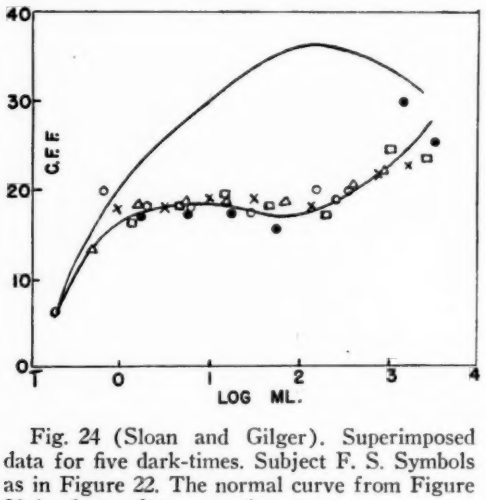

Fig. 24 (Sloan and Gilger). Superimposed data for five dark-times. Subject F. S. Symbols as in Figure 22. The normal curve from Figure 23 is shown for comparison.

increase in dark-time from 10 percent to 90 percent was 19.8 and 20.0 cycles per second. The two patients on Tridione showed increases of only 10.9 and 14.0 cycles per second. The results suggest that the rate or extent of recovery taking place during the dark phase was decreased in some way by Tridione.

The effects of Tridione on sensitivity to flicker, demonstrated in these studies, may be summarized as follows. (1) With increase in intensity of both test field and surround, c.f.f. at first increased, but more slowly than normal. When an intensity of about 300 ml. (log I-2.5) was reached, c.f.f. decreased with further increase in intensity. (2) When the surround was maintained at a constant low brightness and only the test field was increased in intensity, a similar decrease in c.f.f. occurred at intermediate intensities. At still higher intensities, however, the c.f.f. increased again and approached a normal value at an intensity of 3 log units or greater. Impairment in foveal sensitivity to flicker at high intensity was greatest, therefore, when a large area of

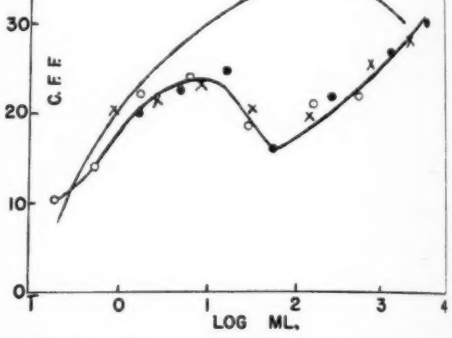

Fig. 25 (Sloan and Gilger). Superimposed data for three dark-times, 90, 50, and 10 percent. Subject R. DeC. Symbols as in Figure 22. The normal curve from Figure 23 is shown for comparison.

the surrounding retina was also exposed to the high intensity. (3) With increase in the relative length of the dark phase of the flicker cycle, the increase in c.f.f. was not as great as that observed in normal subjects. (4) The abnormalities in flicker

TABLE 2

CHANGE IN C. F. F. WITH CHANGE IN LENGTH OF DARK PHASE OF FLICKER CYCLE

Increase in Dark-Time from 10% to	Cycles Per Second			
	Normal 1	Normal 2	F. S.	R. DeC.
25%	8.2	6.1	5.5	—
50%	13.2	12.4	8.3	11.1
75%	16.5	14.3	9.3	—
90%	19.8	20.0	10.9	14.0

sensitivity observed in patients on Tridione do not appear to be closely related to the impairment in visual acuity, brightness and color discrimination observed in these patients. Flicker sensitivity may, for example, show marked impairment under experimental conditions in which visual acuity is not affected. One patient, F. S., with very marked defects in the flicker tests showed only slight impairment in the other group of tests.

VI. Additional studies

Before Tridione therapy was commenced, external, ophthalmoscopic, and slitlamp examinations were made on each patient. Most of the patients showed a faint lenticular haze and slight retinal vascular changes of an arteriosclerotic or arteriolar sclerotic nature. Other than these, no pathologic findings were present in the seven patients studied intensively. During the time which these patients were followed, there was no change in these findings except in one case where there was a definite slight increase in fine cortical opacities during the course of nine months. All the patients studied in the previous tests had corrected visual acuities of 20/20 or better in each eye, and read Jaegar 1 with correction.

Two additional patients on Tridione died from other causes, one while on therapy and the other 48 hours after it was discontinued. Because of their bedridden state, extensive studies of visual function had not been made. Sections of the posterior segments of these eyes were obtained and studied with the help of Dr. Jonas S. Friedenwald. As was anticipated, the delay in fixing the eyes due to the time required to secure the autopsy permits resulted in sufficient autolysis to mask any slight changes in the nerve cells and fibers which might have been seen with special staining techniques. No pathologic findings were present except those diagnosed ophthalmoscopically prior to therapy with Tridione and those due to the terminal systemic disease. The eyes of one of the patients who died of uremia showed on microscopic examination: "Slight septic choroiditis; retinal arteriosclerosis." Retinal arteriosclerosis was the diagnosis made before Tridione was given. The other patient died from bronchogenic carcinoma. Ophthalmoscopy before Tridione revealed pallor of the discs, O. U., and there was no observed change during therapy. The eye-pathology diagnosis was: "Slight septic choroiditis; partial optic atrophy."

Subjective sensations of the patients while on therapy were of interest. While adapting to a high intensity of illumination, most reported that "white clouds" were passing in front of their eyes. Occasionally the clouds would roll away so that they could see better and then would close in for a short time again. Three patients complained of erythropsia in outdoor illuminations; this disappeared on continued use of the drug. Our patients found that their subjective symptoms were alleviated by wearing dark glasses in outdoor illuminations.

Summary and Conclusions

The significant effects of Tridione on visual function demonstrated in this study may be summarized as follows:

1. Acuity, brightness sensitivity, color discrimination, and sensitivity to flicker showed temporary impairment in all patients tested, when both the foveal test field and a surrounding area of 6 to 10 degrees were illuminated to a high brightness. While these findings all point toward impairment in function of the foveal cones at high brightnesses, supplementary tests indicated that the defect was not a localized central scotoma but involved cone function throughout the entire retina.

2. With continued exposure to the high brightness there was gradual improvement in visual function. In 5 of 7 patients, acuity and brightness discrimination reached normal values after about 10 minutes. Sensitivity to flicker, although it improved, continued to show significant impairment after long adaptation to the high brightness in patients who had recovered normal acuity and normal brightness sensitivity.

3. Two of the seven patients showed a lasting impairment of both acuity and brightness sensitivity at 2,000 ml. Tests of acuity at brightnesses below 2,000 ml. indicated that significant lasting impairment may extend to brightness levels of 50 ml. or less.

4. All patients showed a temporary impairment in acuity and in brightness sensitivity at 2 ml. after previous adaptation to 2,000 ml. None showed lasting impairment after adaptation to the low brightness.

5. Impairment in foveal sensitivity to flicker at high intensities was less marked when the brightness of the surrounding fields was 1 ml. and only the 1-degree test field was of high brightness.

6. Increase in the length of the dark phase of the flicker cycle produced less than the normal increase in sensitivity to flicker at the fovea. This was true at low as well as at high brightnesses of the test field.

7. The findings in patients studied for more than three months while on Tridione indicate that tolerance to the visual side effects develops with continued medication. Patients reëxamined after the drug was discontinued showed no evidence of any visual impairment after 10 weeks without Tridione.

The action of Tridione on the visual mechanism probably does not occur posterior to the chiasm, since exposure of one eye to a high brightness does not produce these effects in the unexposed eye. If the action were at the level of the optic nerve, it is unlikely that cone fibers alone would be affected. It seems probable, therefore, that the drug produces its effects at the retinal level. For the most part, the phenomena suggest that the neural layers of the retina rather than the photochemical processes are involved. Studies on animals of the effects of Tridione, using the electroretinogram, measuring the optic-nerve discharges, and so forth might, therefore, be of aid in explaining the mechanism of the visual defects.

Johns Hopkins Hospital (5).

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THE EFFECTS OF DI-ISOPROPYL FLUOROPHOSPHATE VAPOR ON THE EYE*

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The fluorophosphates have an eserine-like effect, increasing the activity of the parasympathetic system. In the eye, this is manifested in a pronounced miosis, reduction of the intraocular pressure, conjunctival hyperemia, aching of the eyeball, and mistiness of vision, the latter effect being due in all probability to increased tonus of the ciliary muscle. General effects include tightness in the chest, headache, rhinorrhea, and diarrhea.

Recent reports of the effect of di-isopropyl fluorophosphate (D.F.P.) on the eye and its use in the treatment of glaucoma have been published by Leopold and Comroe,[1,2] and by McDonald.[3] An investigation into the potentialities of D.F.P. vapor as a chemical-warfare agent was undertaken by us during 1943.* With the lifting of security regulations it was thought wise to publish it in part since it contains certain basic observations on the effects of this compound on the eye.

Experimental

1. Production of the vapor concentration. Air containing di-isopropyl fluorophosphate vapor was obtained with the constant-flow device.

Owing to the lengthy analytical procedure, no analysis of the vapor concentration was carried out immediately before exposure, as with our earlier ex-

* This work was carried out under the Physiological Section (A. Fairley, head) of the Chemical Defence Experimental Station, Porton, England (Porton Report 2592). Since these experiments were designed primarily to assess the degree of visual impairment, no observations on the reduction of intraocular pressure were made.

periments, but samples of the flow were taken after each exposure for subsequent analysis. This procedure was justified by the comparatively minor eye effects which were expected and by the high degree of predictability of the vapor concentrations from the tap settings of the instrument. Very rarely did the actual dosage differ from that intended by more than a few percent. Difficulty was encountered with the decomposition of the di-isopropyl fluorophosphate presumably through the agency of moisture and alkali from the soda-glass beads in the bubbler. Bubblers were constructed with Pyrex bodies and with phenolformaldehyde resin chips in place of the beads, and the air used in the constant-flow device was dried over calcium chloride before it entered the bubbler. The stability of the di-isopropyl fluorophosphate was greatly enhanced by this procedure and consistent values for the saturation concentration could readily be calculated from the results. At 13.2°C., a saturation concentration of 3,470 mg./m^3, corresponding to a vapor pressure of 0.337 mm. Hg, was observed.

2. Determination of the vapor concentration. The concentrations of di-isopropyl fluorophosphate in the vapor were estimated using the method for fluorine determination. Good reproducibility was obtained.

3. Exposure to the vapor. A modified respirator face-piece, which permitted the passage of vapor over the eye while enabling the individual to breathe pure air, was employed.

Both eyes were exposed, except in a few instances where corneal and iris changes were being observed. Exposure times were kept constant at five minutes and the concentrations varied in different experiments from 8 to 50 mg./m^3, giving dosages (Ct)* in the range 40 to 250 mg. min/m^3.

4. Clinical examinations. Parasympathetic stimulation may possibly influence: (a) Pupil size; (b) visual acuity; (c) the near point of accommodation; (d) the threshold of scotopic or rod vision by virtue of the diaphragmetic action of the iris; (e) the tone of the superficial and deep vascular layers of the eye, causing conjunctival hyperemia and uveitis.

Finally, the general toxic action of di-isopropyl fluorophosphates might cause corneal changes such as edema and infiltration (f). The various factors (a) to (f) were investigated as follows:

Factors investigated

(a) Pupil size. The individual was placed in a dimly illuminated room such as to produce a brightness of about 1.15 equivalent foot-candles on the yellowish-white walls; he was told to look at the distant wall (6 meters away) and a scale was held in front of the eye and the pupillary diameter measured. In one experiment photographic methods were also used and these will be described later.

(b) Visual acuity. Vision at 6 meters was measured with a Snellen chart illuminated to give a brightness of its white background of 17 foot-candles, and the lowest row of letters which could be read was noted.

(c) Accommodation. The near point of accommodation was determined fairly crudely by holding a meter scale perpendicular to the malar bone and instructing the individual to bring a test-type card closer and closer until the fine type was blurred; he was then told to move the card back until he could just read the type distinctly, and the distance from the malar bone to this final position was recorded.

* "Ct" is used in chemical warfare to express unit dosage. Ct denotes the concentration of the gas in milligrams per cubic meter times the period of exposure in minutes.

TABLE 1

PUPIL SIZES* OF SUBJECTS IN DIMLY LIGHTED ROOM BEFORE AND AFTER EXPOSURE TO DI-ISOPROPYL FLUOROPHOSPHATE VAPOR

Subject	Dosage	Before Exposure	1 Hr. Later	24 Hrs. Later	48 Hrs. Later	72 Hrs. Later
A	40	R 4 L 4	R 2.5 L 1	R 2 L 1.5	R 3 L 2	R 3 L 2.5
B	40	R 6 L 6	R 3 L 1.5	R 2 L 1	R 2.5 L 1	R 4 L 2.5
C	40	R 6 L 6	R 2 L 2	R 2 L 1	R 2.5 L 1.5	R 3 L 2
D	80	R 5 L 5	R 2 L 1.5	R 2.5 L 1.5	R 3 L 2	R 3 L 2
E	80	R 5 L 5	R 2.5 L 2	R 2.5 L 1.5	R 2 L 1	R 3 L 2
F	80	R 4 L 4	R 2 L 1.5	R 1 L 1	R 1 L 1	R 1 L 1
G	116	R 5 L 5		R 2 L 2	R 3 L 2	
H	116	R 5 L 5		R 2.5 L 1.5	R 3 L 1.5	
K	116	R 5 L 5		R 1.5 L 1.5	R 1.5 L 1.5	
L	158.5	R 5.5 L 5.5	R 1.5 L 1.5		R 1 L 1	R 1.5 L 1.5
M	158.5	R 5 L 5	R 1.5 L 1.5	R 2 L 2	R 2 L 2	R 2 L 2
N	191	R 4 L 3	R 1 L 1	R 1.5 L 1.5	R 1.5 L 1.5	R 2.5 L 1.5
O	191	R 3 L 3	R 1 L 1	R 1.5 L 1.5		R 1 L 1

* *Diameter of pupil in mm.*

The mean of three determinations on each eye separately was taken. If the individuals had any refractive error, this was corrected with appropriate lenses before the test was made.

(d) Scotopic visual threshold. The individual was light adapted for five minutes with a bright source of light in a dark room. The light was switched off and immediately afterward the threshold of light sense was recorded continuously for half an hour on the Craik Adaptometer.

(e) Vascular tone. The conjunctiva was examined for reddening, and the fundus observed with the ophthalmoscope. In selected individuals, a slitlamp examination of the iris was made.

(f) Corneal changes. Selected individuals (exposed to high dosages) were examined under the slitlamp.

RESULTS

(a) Pupil size. (See Table 1). In general, miosis began about 10 minutes following exposure; in most cases it had reached its maximum in 24 hours, although in dosages above 116 mg. min/m^3

full constriction was present one hour after exposure. The miosis usually remained constant for 48 hours after which it began to abate somewhat. In the higher dosages (above 116 mg. min./m³), there was usually no sign of relaxation of miosis even after 72 hours. It was impossible to follow up all the subjects to ascertain how long their miosis lasted, since they were military personnel and were allowed away from their units for a few days only. However, in some preliminary experiments, it was noted that the pupils did not regain their normal size in the light for five to six days, even with moderate dosages.

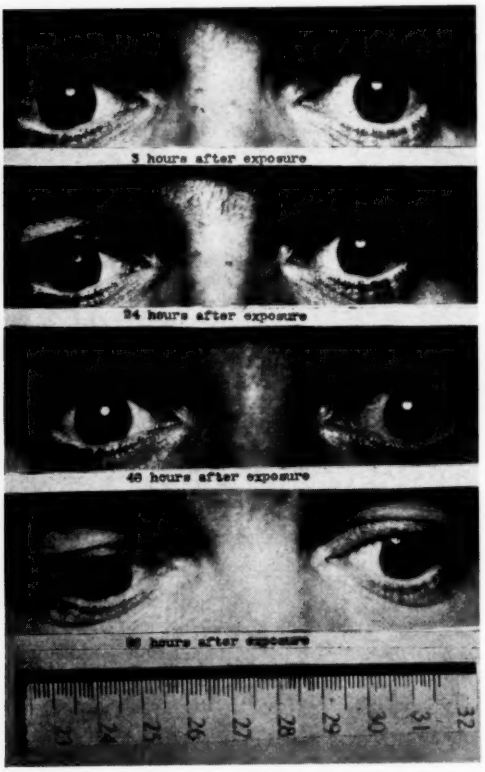

Fig. 1. (Aldrige, Davson, *et al.*). Pupil sizes after dark adaptation. Only the left eye has been exposed to D.F.P.

The miosis following D.F.P. exposure may be largely due to an exaggeration of the normal light reflex following the inactivation of cholinesterase; if this were true it might be expected that the miosis would relax after, say, 30 minutes to one hour in the dark. At the end of some of the dark-adaptation tests, at which time the individuals had been in the dark for some 30 minutes, an attempt was made to measure the pupils with the aid of a dim red lantern. The impression was gained that within a few hours of the exposure no relaxation of miosis occurred; whereas, after 48 hours it appeared that some increase in pupil diameter took place during dark adaptation. A more accurate experiment was carried out as follows:

Fig. 2 (Aldrige, Davson, *et al.*). Subject Q. A flashlight photograph of 1/30,000-second exposure, taken 48 hours after the eye was exposed to D.F.P. The eye, dark adapted for 10 minutes, shows miosis and engorgement of the conjunctival blood vessels. Only the left eye was exposed to D.F.P.

The left eyes only of three men were exposed to a dosage of 100 mg. min./m³, and two hours later they were kept in a dark room for one hour; their eyes were then photographed in the dark by flashlight of 1/30,000-second duration. The same procedure of dark adaptation and flashlight photography was repeated 24, 48, and 96 hours later. The results are shown in Figure 1.

There is no doubt that the miosis can be pronounced, even after one hour's dark adaptation, and that it persists to some extent for as long as 96 hours after exposure with, however, a progressive relaxation from day to day. The persistence of the miosis for one hour in the

TABLE 2

VISUAL ACUITIES* OF SUBJECTS IN BRIGHT LIGHT BEFORE AND AFTER EXPOSURE TO DI-ISOPROPYL FLUOROPHOSPHATE VAPOR

Subject	Dosage	Before Exposure	1 Hr. Later	24 Hrs. Later	48 Hrs. Later	72 Hrs. Later
A	40	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4
B	40	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S.	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4
C	40	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4
D	80	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/5 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4
E	80	O.D. 6/12 O.S. 6/4	O.D. 6/12 O.S. 6/6	O.D. 6/12 O.S. 6/5	O.D. 6/12 O.S. 6/6	O.D. 6/12 O.S. 6/9
F	80	O.D. 6/4 O.S. 6/5	O.D. 6/4 O.S. 6/5	O.D. 6/4 O.S. 6/5	O.D. 6/4 O.S. 6/5	O.D. 6/4 O.S. 6/5
G	116	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	
H	116	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	
K	116	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/5	O.D. 6/4 O.S. 6/4	
L	158.5	O.D. 6/9 O.S. 6/9	O.D. 6/5 O.S. 6/5	O.D. 6/6 O.S. 6/6	O.D. 6/6 O.S. 6/6	
M	158.5	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4	O.D. 6/4 O.S. 6/4
N	191	O.D. 6/36 O.S. 6/12	O.D. 6/36 O.S. 6/12	O.D. 6/36 O.S. 6/12	O.D. 6/36 O.S. 6/12	
O	191	O.D. 6/36 O.S. 6/6	O.D. 6/36 O.S. 6/6	O.D. 6/36 O.S. 6/6	O.D. 6/36 O.S. 6/6	
P†	250	O.D. 6/9 O.S. 6/12	O.S. 6/12	O.S. 6/12	O.S. 6/12	
Q†	250	O.D. 6/5 O.S. 6/4–1	O.S. 6/4–3	O.S. 6/4–3	O.S. 6/5	
R†	250	O.D. O.S. 6/6	O.S. 6/6	O.S. 6/6	O.S. 6/9	

* *Visual acuity (corrected).*
† O.S. only exposed.

complete absence of light stimuli tends to confirm the belief, generally held, that the pupil size is normally controlled by a balance between tonic constrictor and dilator impulses; the potentiation of the tonic-constrictor impulses by the eserine-like action of di-isopropyl fluorophosphate is sufficient to maintain a pronounced miosis even in the absence of light stimuli.

(b) Visual acuity. (See Table 2). There was practically no impairment of visual acuity among the 16 subjects used for this test.

(c) Accommodation. (See Table 3). The effects of dosages of D.F.P. ranging from 40 to 191 mg. min./m³ on the position of the near-point of accommodation were noted. It was found the near-point moved inward a few centimeters in all cases, a finding which suggests that there is an increased development of tension in the ciliary muscle during accommodation; the absence of any serious impairment of distance vision, however, indicates that there is no uncontrollable spasm of this muscle with the concentrations employed.

(d) Scotopic visual theshold. (See Table 4). The threshold brightness required to stimulate the light sense of dark-adapted individuals before and after exposure to D.F.P. was recorded. In all cases the threshold increased one to two hours after exposure, and later tended to return to normal. If the pupil size before exposure were 6 mm. and after exposure 1.5 mm. in diameter, the amounts of light entering the eye in the two conditions would be in the ratio of about 16 to 1 and one would expect the thresholds to be raised in this proportion. In actual fact so large an increase was never found, the maximum effect being a tenfold rise. The effects of instillation of two drops of 0.5-percent eserine and of 1.2-percent homatropine hydrobromide on threshold brightness were then studied, it being found that eserine has a comparable effect with that of D.F.P. On the other hand a slight reduction in the visual threshold occurred with homatropine as would be expected with a dilated pupil.

(e) Vascular tone. (See Figure 2).

TABLE 3

EFFECT OF DI-ISOPROPYL FLUOROPHOSPHATE VAPOR ON THE NEAR-POINT* OF ACCOMMODATION

Subject	Dosage	Before Exposure	1 Hr. Later	24 Hrs. Later	48 Hrs. Later	72 Hrs. Later
A	40	R 19.5 L 19.5		R 16 L 13.5	R 15 L 18.5	R 17.5 L 16.5
B	40	R 12.5 L 13		R 11.5 L 7.5	R 9.5 L 8	R 12.5 L 14
C	40	R 15. L 14.5		R 13 L 13	R 13.5 L 12	R 15 L 12
D	80	R 21 L 21		R 16 R 12	R 18.5 L 13	R 17.5 L 12
E	80	R 12 L 12		R 6.5 L 6	R 7 L 6	R 7.5 L 6
F	80	R 11 L 10		R 9 L 10	R 11 L 9	R 9.5 L 8
L	158.5	R 16 L 14	R 9.5 L 10	R 9.5 L 10		R 13 L 13
M	158.5	R 17 L 16.5	R 15 L 12.5	R 12 L 11	R 12 L 11	R 12 L 11.5
N	191	R L 17.5	R L 15	R L 13.5	R L 17.5	
O	191	R L 16	R L 14.5	L 14	L 17	

* *Near-point of accommodation in cm.*

TABLE 4

VISUAL THRESHOLDS* OF DARK-ADAPTED SUBJECTS BEFORE AND AFTER EXPOSURE TO DI-ISOPROPYL FLUOROPHOSPHATE AND CERTAIN DRUGS

Subject	Dosage mg. min/m.³	Before Exposure	1–2 Hr. After	24 Hrs. After	48 Hrs. After	72 Hrs. After
K	116	0.8	8.0		2.5	
H	116	2.0	7.0		3.0	
G	116	0.8	4.0	0.9		0.4
L	159	0.3	0.9	5.0	2.0	1.0
N	191	0.5	1.0	1.0	1.0	
O	191	1.0	8.0	8.0	5.0	
S	Eserine	1.5	10.0	1.0		
T	Eserine	0.9	3.5	2.5		
G	Eserine	0.4	1.5			
U	Homatropine	0.9	0.8	0.7		

* *Threshold brightness in equivalent foot-candles.* $\times 10^6$.

Subjects exposed to dosages of 100 mg. min./m³ and above generally showed hyperemia of the conjunctival vessels, the sign appearing some 48 to 72 hours after exposure with dosages up to 191 mg. min./m³ (although in one case it appeared within 24 hours). With a dosage of 250 mg. min./m³, the hyperemia was much more severe and was manifest within 24 hours of exposure. With this dosage, a marked congestive iritis developed in three of the volunteers, as evidenced by the presence of dilated iris vessels, and cells in the anterior chamber. This was present for one day only, and responded to instillations of homatropine.

The marked miosis of subjects exposed to D.F.P. vapor precluded a careful ophthalmoscopic study, except in the instances where the miosis was abolished with a mydriatic. No changes were noted.

(f) Corneal changes. No changes were observed under the slitlamp even with the highest dosages.

(g) Subjective symptoms. The subjective symptoms volunteered by the individuals exposed to the higher concentrations of vapor consisted in mistiness of vision, aching of the eyeballs, and difficulty in seeing in dim light. The symptoms began to clear up on the third day following exposure.

DISCUSSION

The results described in the earlier sections of this report speak for themselves. Several points emerging from this work will, however, bear comment. The most dangerous effect of D.F.P. vapor on the eye is clearly the congestive iritis caused by dosages of 250 mg. min./m³. Associated with the iris changes was a marked conjunctival hyperemia, both signs appearing some 24 hours after the exposure. With more moderate dosages of 100 to 200 mg. min./m³, conjunctival signs only were observed, and these appeared, with one exception, 48 hours after exposure. The cause of these delays is not easy to find—it may be that the continued accretion of unhydrolysed acetylcholine eventually causes sufficient stimulation of cholinergic dilator fibers to overcome the

normal constrictor tone of the eye vessels, but this is mere speculation.

The effects of the vapor on the accommodative apparatus were slight, suggesting merely the development of a greater than normal tension in the ciliary muscle during accommodation.

As one would expect, the diaphragm effect of the miosis causes a rise in the threshold of night vision, similar in magnitude to the effects described in the literature.

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SOME METHODS OF LID REPAIR AND RECONSTRUCTION

IV. Total reconstruction of the upper lid*

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Trauma which destroys the entire upper lid and leaves the lower lid intact is a rare phenomenon. Spaeth[1] has labeled this type of case "the accident of an accident" and states, "No case has ever presented itself to the author in which the upper lid was alone involved and completely destroyed." This report is of interest, therefore, because it concerns just such an injury.

Case report

T. B. was wounded on April 13, 1945, while fighting in northern Luzon. He sustained a penetrating wound of the right upper lid and the right eyeball, fractures of the right orbital bones, and a laceration of the right frontal lobe of the brain. The following day the eye was enucleated, the upper part of the orbit exenterated and the brain wound debrided. Recovery was uneventful, and the patient was returned to this country for further plastic surgery.

On admission to the hospital here, examination showed the upper lid to be completely absent. The whole socket except for the palpebral portion of the lower lid near the margin was lined with granulation tissue. The lower lid was intact but entropic. By some trick of fate the caruncle was spared. This was a welcome windfall as the final cosmetic result is always better when the caruncle is present (fig. 1). The repair was made as follows:

First Stage. A pedicle flap (1.5 cm. wide and 8 cm. long) was raised from the skin of the right forehead with the lower 4 mm. including the hair of the brow (fig. 2a). This was delayed for two weeks. Fourteen days later the skin edges around the upper orbit were freshened and the granulation tissue covering the

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upper half of the socket carefully scraped away. The skin of the naso-orbital angle was undermined and mobilized. The pedicle flap from the brow was raised again, rotated down, and sutured above

Fig. 1 (Fox). Condition before operation showing total loss of the right upper lid. Socket is lined with granulation tissue. Note entropion of right lower lid and sparing of caruncle.

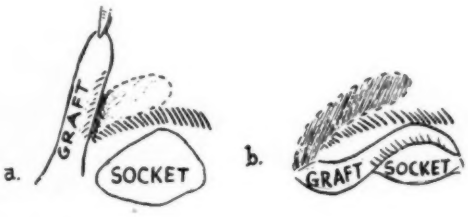

Fig. 2 (Fox). Diagram of procedure in first stage of repair. (a) A pedicle graft is raised from the forehead to include hair of brow at lower margin for the cilia line of the reconstructed lid. (b) After a delay of 14 days, the pedicle is raised again, rotated down, and sutured to the freshened skin edge below the brow.

and medially to the skin below the brow with interrupted sutures of 4-0 braided black silk (fig. 2b). The wound above the brow was closed with 4-0 plain catgut, subcuticular, and 4-0 black-silk skin sutures. The socket was stuffed with vaseline gauze and the graft pressed against the upper posterior socket wall to insure adequate blood supply. A firm supportive dressing with bandage was applied. The graft "took" well and the sutures were

Fig. 3 (Fox). Ten days later, before removal of the sutures. The graft has taken well.

removed on the 10th day after operation (fig. 3).

Second Stage. Six weeks later the graft, now obviously healthy and viable, was dissected away from the socket wall, and the socket itself was lined with a split skin graft taken from the inner aspect of the right arm. The method used here was described in a previous report published in the JOURNAL.[2] Figure 4 shows the reconstructed socket with a conformer in place.

Third Stage. Five weeks later the scar below the brow was excised and subcutaneous tissue resected to thin out the lid and give it a more normal appearance. (It should be remembered that brow skin is thicker than the skin of a normal lid). At the same time a free graft was taken from the left upper lid and planted in the bed thus prepared for it in the recon-

Fig. 4 (Fox). The graft is dissected away from the socket wall, and the socket is lined with a split skin graft. Conformer in place.

Fig. 5 (Fox). Lid graft is thinned out, and the free skin graft from the left upper lid is added to the right upper lid to widen it and to bring lid edge down parallel with lid of the other eye.

structed right lid. In this way the lid was widened and its edge brought down to approximately the same level as the left upper lid (fig. 5).

Five weeks later the entropion of the lower lid was corrected by exposing the tarso-orbital fascia and external canthal ligament and incising them sufficiently in the lower orbital quadrant to cause relaxation of the lid. This corrected the entropion too well (fig. 6) and subsequent tightening of the relaxed lower lid appeared necessary.

Discussion

Many methods of repair are open to the surgeon in a case of this sort. These include, among others, the use of a tubed graft from the neck, rotated pedicles from the temple, cheek, and lower lid, and multiple free grafts of skin and cartilage. It is believed, however, that the method chosen here is the simplest available for a complicated case, for the following reasons:

1. There is comparatively little scarring as a result of the surgery, since most of the donor site is buried in the hair of the brow. For cosmetic reasons it is always best to have scars running parallel with the orbital margin whenever possible; a tubed graft or temporal pedicle would therefore have been more conspicuous.

2. The blood supply, and therefore the viability of the graft, is more certain with a pedicle than with a free graft, especially if delayed.

3. Since brow skin is at least as thick as the whole lid, the single layer was enough. Indeed, this single layer had to be thinned out to make the repaired lid conform to the other upper lid.

4. In a case of this sort there is no question of restoring function because there has been too much destruction. The reconstructed lid is immobile no matter what method is used. The aim of surgery here can only be cosmetic restoration, and the result is just about as good (or bad) as can be obtained with any other technique.

5. Because it is the simplest procedure technically, it is preferable.

In cases in which there is so much destruction, the question always arises as to whether the result is worth the effort. Some surgeons of long experience, whose opinions are valuable, feel that total lid reconstructions are never justified, because the patient is so often dissatisfied with the final result. Certainly patients should be warned before operation that one cannot reconstruct a complete lid to match the normal lid in every respect. One

Fig. 6 (Fox). Prosthesis in place after correction of entropion of right lower lid. "Stary" appearance is due to the sclera showing between the lower lid and limbus. This requires further correction.

must expect and be satisfied with a good deal less than perfection. If one succeeds in reconstructing a lid which is presentable and not conspicuous, the result is adequate.

In this case, lid and socket reconstruction made retention of a prosthesis possible and the patient was not condemned to wearing a patch for the rest of his life. The lid, although far from perfect, was sufficiently presentable so that the patient was content and did not clamor for more surgery. He was even reluctant to have the lower lid pulled up for fear of "spoiling" the result.

Summary

A method of total upper lid reconstruction by the combined use of a rotated pedicle and free graft is presented.

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TECHNICAL METHODS FOR THE 1/2,000 FIELD*

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The study of the central field on the tangent screen is of great importance in ophthalmology and neurology. In those conditions where the field changes are marked, they are easily elicited with large visual angles and the technique is not very complicated. Thus, in marked papilledema the enlargement of the blind spot may easily be mapped out with a 10-mm. white test object at two meters. Also in cases of complete hemianopia, where the scotomatous areas are very dense, sufficient information may be elicited even by confrontation. However, in working with a large neurologic and neurosurgical staff one sees many cases with either minimal or questionable visual-field changes.

In such cases, more accurate information can be obtained by using a very small visual angle, such as the 1-mm. white test object at 2,000 mm. The visual angle subtended by this combination is 1.72 minutes and is one of the smallest visual angles that is still compatible with practical clinical use. Because of the small size of this angle, this test must be reserved for patients with good enough vision to see the test object in a reasonably fair-sized portion of the field.

This small visual angle is especially useful in diagnosing cases of early lesions in which the 5/330 or 1/330 fields will show little or no defect. In such cases, the 1/2,000 test will bring out minimal changes. Thus, in early chiasmal interference, one may get a definite upper temporal slant with a 1/2,000 test, and little to no change with the 1/330 test on the perimeter. Many such cases are illustrated by Traquair.[1] In order to demonstrate this point, two cases have been selected from the neurosurgical service of Montefiore Hospital.

* This work was done in the Ophthalmological Laboratories of Montefiore Hospital, and was aided by the William L. Hernstadt Fund.

Case reports

Figure 1A shows the visual fields in a case of pituitary adenoma with chiasmal interference. The right eye shows only a slight peripheral, relative defect, temporally, for 1/330 white. The 1/2,000 test, however, shows almost complete loss of the upper temporal quadrant and beginning loss of the lower temporal quadrant.

Figure 1B demonstrates a case where the peripheral fields for 2/330 were normal, while the 1/2,000 test showed a definite bitemporal hemianopia. The latter case had very dense bitemporal, paracentral scotomas preoperatively and a reduction in vision in the right eye to 6/200. X-ray studies showed an enlarged sella turcica. One week after the removal of a craniopharyngioma by Dr. Davidoff, vision returned to 20/20. At this time the peripheral field for 2/330 white was normal in both eyes while the 1/2,000 test still brought out the bitemporal defect (fig. 1B).

In some cases, the actual existence of a tumor was suggested by using a small visual angle when it was missed with a larger one. To quote Traquair, "In clinical work, the examination with 1/2,000 white is one of the most important tests and is indispensable. To omit the 1/2,000 white test is comparable to examining the central vision with a chart which has no line below 6/12ths."[1]

Therefore, the study of the visual field with the 1-mm. white at 2,000 mm. is important in bringing out early or minimal defects in the visual pathways. However, the use of this small visual angle presents many technical difficulties, some of which will now be discussed.

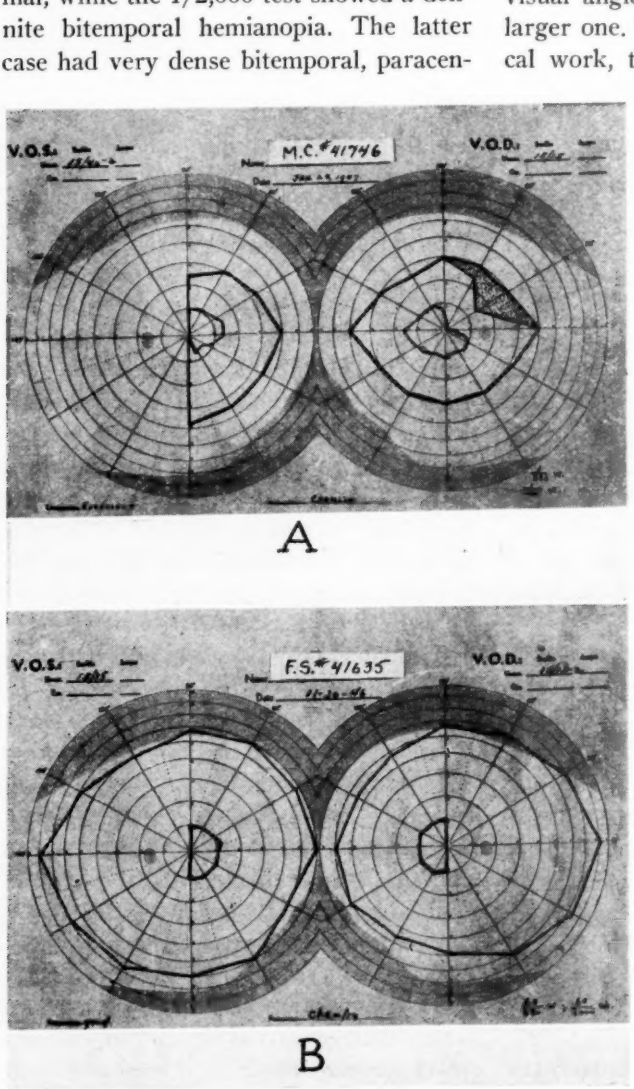

Fig. 1 (Chamlin). (A) Case of pituitary adenoma. Right field for 1/330 white shows only relative defect in upper temporal field, while 1/2,000 test shows almost complete loss of upper temporal quadrant and beginning loss of lower temporal quadrant. (B) Case of craniopharyngioma one week after removal. The fields for 2/300 white show no changes but the fields for 1/2,000 white show a very sharply defined bitemporal hemianopia.

Technical difficulties

Patient

One must be careful in selecting the proper type of patient for this test. It is easiest to do this test if the patient has good visual acuity and becomes more difficult with impairment of central vision. The patient must show evidence of understanding the test fully. Certainly, a patient whose mentality is dulled by intracranial lesions or preoperative medication is not fit for this test. He must be intelligent enough and dependable enough to distinguish the small white-headed target from any distraction and he must understand fully the need for constant fixation. It takes but a fleeting, almost imperceptible shift of the eye to look at the moving test object instead of the fixation point, thereby giving erroneous readings.

Technique

Before starting the test, the test object and carrier are shown to the patient at close range, and it is explained to him that he must recognize the test object and not the adjacent parts of the carrier. The shaft of the Berens pin or the wire of the Evans bead must be pointed out to the patient so that he does not confuse them with the tiny test object.

The patient is made comfortable with a head and chin rest and one eye is carefully covered. The head and chin rest should be adjusted to the level of the patient's face so that he will not have to bend his head forward or backward. Excess inclination of this nature may give erroneous readings in the upper and lower fields. The patient should wear his distance correction, especially when visual acuity is poor without it. With glasses, care must be taken that neither the frame nor bifocal segment interferes with the field. If necessary, the lenses may be replaced with a large trial-case frame and lens.

It is best to start by using a large test object, such as 10 mm., then 3 mm., and finally 1 mm. In this way, one gradually teaches the patient the general idea of the test. Before recording the readings with the 1-mm. test object, it is well to take several practice readings. Several constant readings must be obtained in a single meridian before considering the patient's responses as reliable.

The field is explored along each of the various meridians. At Montefiore Hospital, the 2-m. screen is marked off in 22.5-degree meridians. The test object is moved toward the center along each of these meridians. The movement should be steady and not too slow. However, it must be slow enough so that the examiner can stop within about ½ cm. from the point where the patient calls the test object as visible. Moving more rapidly may lead to errors. On the other hand, if the movement is much slower, nonexisting scotomas may be falsely recorded. This is so, because a small stimulus such as this one, when viewed indirectly in the periphery of a field for a short period of time, will disappear from view unless it is moved continually so as to stimulate fresh retinal receptor units.[2] Thus, if we move very slowly, the patient may say "I see it, but now it seems to be gone." Of course, one must be careful to differentiate such errors in technique from true scotomas. The area should again be explored with slightly faster motion, and the patient must tell whether or not the white object disappeared for a short distance.

There is no need for using any zigzag motion. This type of motion is unscientific in a test such as this one and in general perimetry, as well. The zigzagging gives the over-all effect of a larger test object and subtends, therefore, a larger visual angle. Such an error would give a larger field and nullify the accuracy of this test. Furthermore, in zigzagging, the

exact point at which the patient sights the object becomes less definite and, therefore, the findings are less exact.

The black-headed pins are used to mark the points at which the white object is seen. The pins are all dipped in flat black paint to avoid bright highlights. A better method of recording is to dictate to a recording secretary the readings for the various meridians and thus avoid the use of the pins entirely. If any peripheral indentations are mapped out, these abnormal readings must be checked. Furthermore, the immediate surrounding field should be explored so that one or two intermediate readings are made between the 22.5-degree markings. If a small peripheral contracture does not depend on a single reading, the interpretation will be more dependable.

Test objects

A spherical test object has been found more satisfactory than a flat one. The visual angle is so small, and consequently taxes the patient's peripheral vision to such an extent, that a flat test object, if only slightly tilted, would introduce a large error. The test object must be clean and perfectly white. Since the Berens test objects are easily washable, they are satisfactory in this respect. However, the shaft of the pin has a thin, smooth layer of dark paint and, if the test object is used on a carrier that exposes this shaft, a brilliant highlight is thrown off which makes it quite difficult for the patient to distinguish the shaft from the tiny white bead in the peripheral field at 2,000 mm. When the shaft of the Berens pin is exposed, it is best to cover it with a coat of flat black paint, such as is used in photography. Apply the paint in a thick and irregular layer so that the surface will reflect less light.

Test-object carriers

The test-object carriers provided with a Berens set are two in number and are made of metal rods about 3 mm. in diameter. The many test objects are interchangeable. The end of the rod is rounded and contains a groove into which the shaft of the pin fits. The test-object carrier has a highly reflecting surface, thus giving an attractive highlight, particularly at the carrying end of the rod. This highlight is very distracting. In addition, the constant changing of test objects mars the paint and exposes the shiny metallic surface underneath which, of course, makes the carrier useless until repainted. When using these carriers, I cover them with the same kind of flat black paint I use on the pin shaft. If 3-mm. or 5-mm. test objects are being used, these difficulties are less important, but with a 1-mm. test object, they are of great significance. No matter how carefully the metal carriers are painted, they still give a more distinct reflection of light than a painted wooden surface of similar size and shape.

Another difficulty arises in a busy perimetry laboratory where one uses only one or two carriers with several different sizes of test objects. The holder and the shaft of the pin lose their paint rapidly and need frequent replacement. Even if the paint does not come off, the finish becomes undesirably shiny from constant handling. Then, too, when put to constant use, the small white head is easily broken off and is frequently soiled.

For these reasons I use test objects which are permanently mounted in separate carriers made of wooden carpenters' dowels about 3 mm. in diameter. These dowels are very inexpensive and come in lengths of 3 or 4 feet. Each dowel can be broken down into 3 or 4 carriers about 12 inches in length. Since they are thin and flexible, a vibratory motion is trans-

mitted to the test object if they are longer than 12 inches. The vibration is minimized, if one touches the tangent screen with the test object, but this is undesirable because the test object will be soiled, and the tiny bead can easily become enmeshed in the superficial fibers of the flannel.

The dowels are dipped into flat black paint. The shaft of the Berens pin is repainted and is then inserted into one end of the painted wooden dowel. To insert the pin, grasp the shaft with a hemostat near its point and force it into the center at one end of the wooden dowel, sinking it 3 mm. into the wood. If it is sunk less deeply, it may fall out. If it is forced farther into the dowel, the wood is apt to split.

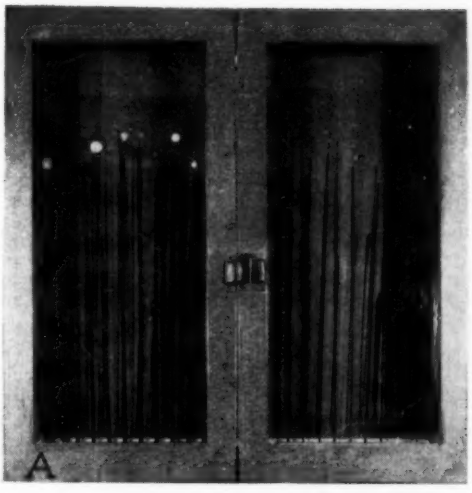

Fig. 2A (Chamlin). Wooden cabinet with glass doors shown closed and attached to wall.

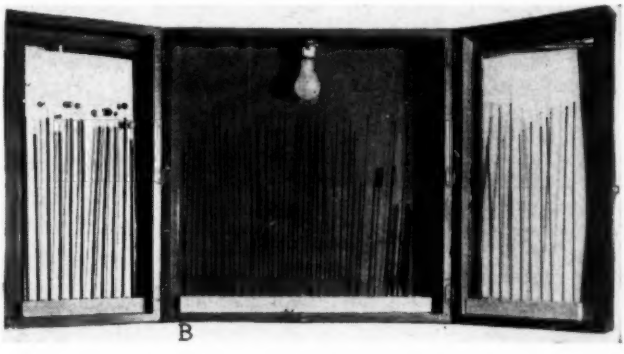

Fig. 2B (Chamlin). Same cabinet as in Figure 2A with doors opened wide showing test-object carriers individually placed and standing upright in the holes in the wooden blocks fastened to bottom of cabinet and its doors. The switch to the light in the cabinet is underneath the box.

After this test object has been attached to its permanent carrier, we try not to touch it or the adjacent parts of the carrier again. A photograph of such a carrier with the 1-mm test object on the Berens pin is shown in Figure 3D. If the pinhead should need cleaning, it can easily be washed with a tiny wet swab and wiped with a dry one.

A 3-mm. dowel is suitable for test objects up to 5 mm. but it is too thin to carry the weight of heavier test objects. When the objects are 10 mm. or more, employ a 6-mm. dowel. (The width of the carrier is no longer as important as it is with the smaller test objects.) These heavier dowels and pin shafts are painted in the same way as the lighter ones, although the finish no longer plays the distracting role that it did with the 1-mm test object.

Heavier test objects are permanently fastened to individual wooden handles to avoid repeated handling of the test object, the pin shaft, and the carrier. By reducing handling, breakage and soiling are minimized.

All of these test objects permanently affixed to their carriers, are kept in a glass-enclosed wall cabinet (fig. 2A). Along the bottom of this cabinet, which is 6-inch deep, there is a block of wood with small holes bored in it, slightly wider than

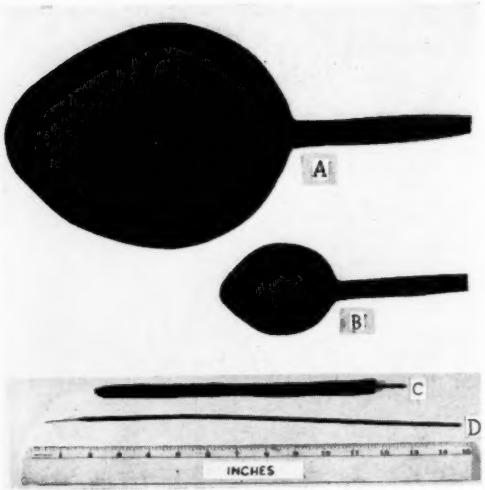

Fig. 3 (Chamlin). (A) Large flannel-covered test-object carrier with 1-mm. test object. (B) Similar test-object carrier but much smaller for use with perimeter. (C) Flannel-covered steel carrier with white test object welded to steel. This is a 2.5-mm. test object. (D) Wooden dowel with Berens pin attached, dowel and shaft of pin being painted matt black. Test object is 1.0-mm. white.

(*Author's note.* Due to the tiny size of the 1-mm. test object, it is not visible in the above photograph. The 1-mm. test object is found in approximately the center of each of the paddle-shaped carriers A and B, also at the end of the shaft of the pin in D. The larger white test object at the end of carrier C is just about visible.)

the diameter of the dowels and 1-inch apart. All the carriers are inserted in this wooden block, with the test objects upward. The two doors closing off the front of the cabinet have a deep frame with a similar block of wood along their lower borders. Thus, when both doors of the cabinet are open (fig. 2B), the entire set of test objects can be checked at a glance, and any one of them can be removed or replaced with ease and without unnecessary handling.

In addition to making the test objects more lasting, the individual handles permit one to use them in rapid succession. For instance, in studying central fields, I frequently use the 1-mm. white, 2-mm. red, and 5-mm. red one after another. If I am not sure that there is diminished vision in an area (that is, a relative scotoma), I can use "rapid comparison." By this, I mean a rapid comparison of vision in the questionable area with that in an area in which the patient professes to have good vision. If this vision is not brought out well with 1-mm. white, it may be brought out with 5-mm. red or 3-mm. red, and it is an advantage to have all these test objects available for rapid use.

An improvement on the combination of the painted wooden handle and the Berens pin would be plastic test objects permanently affixed to plastic carriers, the whole unit being in one piece. The handles of the set I plan to have made are to be of black, unpolished plastic, tapered at the end to which the plastic spherical test object is to be permanently affixed. Such a complete plastic set will eliminate the need for painting and will do away with the occasional breaking off or falling out of the pins from the dowels. Such equipment can easily be cleaned with a damp cloth without the danger of dislocating the pin, as in the wooden holder, and the colors will be permanent.

I have devised several other types of test-object carriers based on the principle that the carrier should simulate the background. The frame is made with flat, thin steel such as is used for stays in women's girdles. The shaft of the Berens pin is soldered to the end of the steel, and the presenting surface of the steel is covered with a length of the same felt or flannel that was used in making the tangent screen. The steel should be no more than ¼ to ½ inch in width, so that the carrier, when overlapped by the material, is no wider than ½ to ¾ inch. A carrier of this width is preferable to a narrower one because the wider piece of flannel, with edges more distinctly separated, is less

distracting. It is also easier to keep a wider carrier more nearly parallel to the plane of the screen, thus avoiding shadow. In cutting the edges of the felt, it is well to bevel them so that the bevelled edges will face the screen and not the patient. This is worth while doing because the bevelled edges stand out from the smooth surface of the tangent screen.

The pin is soldered so that only about ⅛-inch of shaft near the head projects beyond the end of the steel blade and is not covered by the felt. Dull black thread, such as Clark's black darning thread, is used to sew this felt to the steel. No stitches should appear on the presenting surface. The small ⅛-inch neck of shaft, between the end of the steel and the pin-head is covered by winding this thread around it. A flat surface is better than a rounded one such as the wooden dowel has, because a flat surface is less likely to give off a highlight. This test object is shown in Figure 3C. These test objects are also kept in an upright position so that the presenting surface and test object do not touch anything when not in use.

Another test object carrier that I have made has its size increased sufficiently to permit the object to be completely surrounded by the exact felt as was used for the screen. The frame for this carrier is fashioned from a sturdy steel wire, about ⅛ inch in diameter. This wire is shaped into an oval about 6-inches wide and 9-inches long, with a handle about 5-inches long. A piece of the tangent-screen felt is stretched tautly over it. All of the stitching appears on the nonpresenting surface. The handle is also covered with the same felt. This carrier resembles a large ping-pong paddle.

The 1-mm. white pin is now grasped with a hemostat at the shaft adjacent to the head, and the remaining length of the shaft is bent until it is at right angles to the smaller portion between the hemostat blades. The pin now looks like the letter "L" with the test object at the end of the shorter limb. The point of the shaft is now plunged through the center of the felt carrier about four inches from its rounded end, and, at the bend, turned at right angles so that the test object presents without any shaft showing, the short neck of the shaft going through the felt at right angles to the plane of the felt. The long end of the shaft now lies on the nonpresenting surface of the felt, and the point is engaged in the superficial fibers of the felt without going through it, and the test object is ready for use. This paddle-shaped test object is shown in Figure 3A.

Before using this test object, tell the patient that he will see a large black surface approaching and that at a certain point, a little white head will appear through the center. By having the test object completely surrounded with black felt for at least 3 or 4 inches in all directions, perfect contrast without interference is achieved. The patient can also recognize the test object more accurately because he knows where the object will appear and keeps his attention there, even though central fixation is well maintained. This gives a more accurate measurement of the field.

The carrier is moved slowly toward the point of fixation and, when the patient makes out the tiny white test object, the carrier is held in position and, with his other hand, the operator holds a black-headed pin over the white test object. The carrier is then withdrawn, and the black-headed pin is pushed into the screen.

The author has found this paddle type of carrier quite satisfactory in mapping out the 1/2,000 field. However, it is unsuitable for use within 2 or 3 degrees of the fixation point, since the surrounding carrier overlaps the fixation point at these limits.

Interpretation of findings

The normal isopter for 1/2,000 white in good illumination is reported differently by various observers, as shown in Table 1. Figures for this table are taken from Traquair.[3]

One must remember that this visual angle is very small and undoubtedly differs with various lighting backgrounds, reflections from test objects, types of carrier, technique of examination, and so forth. Considering all of these factors, it is not at all surprising that there are discrepancies in the findings of these observers. I believe that each ophthalmologist should observe the 1/2,000 field for a small series of normal subjects on his own screen in order to see which of the reported isopters is closest to the average isopter he has found on his own screen. He should then use that reported isopter for the normal.

However, the exact extent of the 1/2,000 field is not really very important. Certainly, because of the discrepancies in different reported normals, little to no importance should be attached to small concentric contractures in this isopter in the absence of other perimetric evidence of interference with the visual pathways. Much more important is localized depression such as a definite temporal or bitemporal slant, homonomous hemianopia, and so forth.

A word of caution regarding the 1/2,000 field in the neighborhood of the blind spot is in order. In most cases, with good lighting, the normal patient will see the test object temporal to the blind spot—usually over a narrow zone of 3 or 4 degrees. Therefore, this area must be explored carefully. In cases of papilledema, in which the blind spot extends as far as the 21- or 22-degree meridian with a 5- or 10-mm. white test object, there may be some additional pericaecal scotoma for 1/2,000 white, thus bringing the caecal area out perhaps to the 25- or 30-degree meridian. This would cause breaking through to the periphery for 1/2,000 white, thereby interfering with the 1/2,000 test in the sense that one might get the impression of a temporal slant; whereas, the depression is really due to the enlarged blind spot.

TABLE 1

Normal isopter for the 1/2000 field as reported by various observers

Observer	Angle In	Object in mm.	Distance in mm.	Field in Degrees			
				Out	Down	In	Up
Walker	1.72	1.2	2,500	20	18	17	17
Sinclair	1.72	1.0	2,000	26	25	26	24
Hefftner	1.72	1.0	2,000	22	18	18	15

Summary

1. The importance of the 1/2,000 white isopter is emphasized as one of the more sensitive and practical tests in quantitative perimetry.

2. Some of the difficulties encountered in the use of this small visual angle are discussed.

3. Suggestions are made for the economical construction and care of individual, permanently fixed holders for small test objects, together with a cabinet for storing them.

4. A new type of carrier, based on a different principle, has been devised.

5. Suggestions are made for the interpretation of the findings for 1/2,000 white.

1840 Grand Concourse (57).

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THE CLINICAL USE OF DI-ISOPROPYL FLUOROPHOSPHATE (D.F.P.) IN CHRONIC GLAUCOMA*

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Recently several articles on the treatment of glaucoma with di-isopropyl fluorophosphate (D.F.P.) have appeared in the literature. D.F.P. is a colorless oily liquid which hydrolyzes rapidly in aqueous solutions with the production of hydrofluoric and di-isopropyl phosphoric acids. Chemically, D.F.P. is unrelated to eserine. Koelle and Gilman have shown that D.F.P. is stable in peanut oil for at least one year when kept in a stoppered bottle at room temperature.[1] They also found no deterioration after autoclaving D.F.P. in peanut oil for one hour at 117°C. From pharmacologic studies on various laboratory animals, it has been learned that D.F.P. inactivates the enzyme cholinesterase. Because of its prolonged action and the rate at which enzyme cholinesterase activity reappears, it has been concluded that D.F.P. acts by irreversibly destroying cholinesterase.[2] When instilled in the eye, it therefore produces symptoms of marked parasympathetic activity which include miosis and contraction of the ciliary muscle.

ANIMAL EXPERIMENTS

Scholz found that, when sublethal or repeated doses of D.F.P. were instilled in the eyes of rabbits under ether anesthesia, tension rose simultaneously with the pupillary constriction and did not begin to return toward normal until approximately 15 minutes later.[3] Histologic examination of eyes removed with the tension elevated showed epithelial blisters on the ciliary processes, engorgement of the vessels, and coagulated protein in the anterior chamber. Scholz and Wallen, however, found that normal human eyes exposed to D.F.P. vapor showed a reduction in tension in all cases but one.[4] The exception showed a slight rise in tension when measured at 10 minutes, but by three hours the tension had fallen below normal. Leopold and Comroe confirmed Scholz and Wallen's findings on normal eyes, but had no exceptions among their 12 cases.[5] Leopold and Comroe demonstrated in human eyes that a 0.1-percent solution of D.F.P. was able to overcome the cycloplegic effect of 4-percent homatropine hydrobromide, and that a 0.2-percent solution of D.F.P. overcame 1-percent atropine sulfate.

CLINICAL EXPERIENCE

The clinical experience of Leopold and Comroe indicated that 0.05-, 0.1-, and 0.2-percent solutions of D.F.P. in oil were suitable for reducing the tension in cases of chronic simple glaucoma.[6] They reported that solutions weaker than 0.05-percent failed to lower significantly the ocular tension in chronic glaucoma and that if a 0.2-percent solution was ineffective, in-

* From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University.

creasing the concentration of D.F.P. was of little value. Because of the prolonged action of D.F.P., Leopold and Comroe cautioned that the frequency of administration of the drug could be determined only by carefully observing the effect on the individual patient. The vast majority of their controlled cases received the drug between the limits of once weekly and twice daily. Most of the cases analyzed by Leopold and Comroe fell into the group classified as chronic simple glaucoma. They reported results on eyes in which pilocarpine and physostigmine had been used unsuccessfully and in which D.F.P. subsequently was used. Of the 52 glaucomatous eyes treated, the use of D.F.P. was considered successful in 36 eyes.

In another report McDonald compared the efficacy of D.F.P. with other miotics in 122 eyes with chronic simple glaucoma uncontrolled by the use of either pilocarpine or eserine.[7] He reported that 57 percent of the eyes in his series were successfully controlled by D.F.P.

Criteria for study

This study is based on the use of D.F.P. in 32 eyes with chronic glaucoma in which the glaucoma previously was uncontrolled by the use of such miotics as pilocarpine (1-percent or 2-percent), eserine (¼-percent), and furmethide (10-percent). The criteria for listing the cases as successfully treated with D.F.P. are the following: (1) The patient should be willing to use the drug sufficiently long to permit a minimum observation period of four months. (2) As a result of treatment, (a) the ocular tension as measured by a Schiøtz tonometer should be maintained at or below 30 mm. Hg; (b) the visual field should show no further loss; (c) vision should be maintained at pretreatment levels provided there is no other obvious reason for a reduction in vision.

Cases were considered unsuccessfully controlled when: (1) The patient was unwilling to continue the medication because of its induced ocular pain or visual symptoms. (2) During treatment, (a) the tension was not controlled at 30 mm. or less; (b) the visual field showed further loss; (c) the visual acuity was reduced.

In this series D.F.P. was used in 0.05- and 0.1-percent concentrations in peanut oil and the frequency of instillation varied from once every two days to twice daily. This is essentially the same concentration and frequency of instillation employed both by Leopold and Comroe and by McDonald.

Types of glaucoma

The types of glaucoma occurring among the 32 eyes in this series and the number successfully controlled with D.F.P. are shown in Table 1.

In these 32 eyes with chronic glaucoma uncontrolled by the more commonly used miotics, D.F.P. was successful in lowering the tension to below 30 mm. Hg (Schiøtz) and maintaining such a reduction for four months in only five eyes—an incidence of 16 percent success. In 27 eyes, the drug was ineffective. In 3 of the 27 failures, the drug was discontinued early because of pain which was so severe that the patients refused further treatment. In the remaining 24 eyes, D.F.P. did not control the tension within satisfactory limits for four months.

McDonald reported that approximately 57 percent of his total cases uncontrolled by previous miotic therapy were successfully controlled by D.F.P. However, he did not give the number of cases of chronic glaucoma alone in his series. His figures, therefore, cannot be accurately compared with the results here reported. Leopold and Comroe's article presented all the pertinent data on the individual cases. Therefore, a further analy-

sis can be made and a comparison with the results here reported is possible. In their series there were 52 eyes with chronic glaucoma which failed to respond to previous miotics. According to their criteria, D.F.P. was successful in 36 eyes and unsuccessful in 16 eyes. When the results of treatment of these 52 eyes are analyzed, using the same criteria which were employed in evaluating the series here reported, there are only 39 eyes which meet the criteria of period of observation and results of treatment. These 39 eyes include 23 apparent successes and their 16 failures. However 8 of the 23 apparent successes do not meet our requirement that the patient be willing to continue the medication. Patients represented by 8 eyes were unwilling to continue the D.F.P. because of either severe pain, blurring of vision, or both. Thus only 15 eyes out of a total of 39, or 38 percent of the chronic cases reported in Leopold and Comroe's article could be classed as successes under the criteria laid down in this paper. In their series it would appear from the available data that the most which could be expected by the use of D.F.P. in chronic glaucoma uncontrolled by the more commonly employed miotics would be control in one of every three cases for a minimum period of four months. The small series here reported gives an even less optimistic view of the situation, only one in six cases being controlled for four months or longer.

Complications of therapy

The complications of D.F.P. therapy which have been mentioned in the literature are: (1) The severe eye or brow ache which is especially common during the first few days of therapy. (2) The blurring of vision caused by ciliary spasm. (3) The occasional increase in tension which D.F.P. may produce.

The following complications occurred in the 32 eyes of our series. Four patients experienced so much pain that in three the therapy was discontinued, and in the fourth, morphine was required the first night to alleviate the pain. This patient was subsequently carried for several days without pain on D.F.P. One aphakic is included among the four which experienced severe pain. Two patients with aphakic eyes also experienced mild pain during the first three days of therapy which was not severe enough to make the patient unwilling to use the medication.

TABLE I

Types of glaucoma occurring in 32 eyes of this series

Type of Glaucoma	No. of Eyes	No. Controlled by D.F.P
Glaucoma Simplex	10 eyes	1
Glaucoma Secondary to Cataract Extraction	8 eyes	2
Glaucoma Secondary to Uveitis	4 eyes	0
Absolute Glaucoma	4 eyes	0
Chronic Congestive Glaucoma	4 eyes	0
Congenital Aniridia	2 eyes	2

Three patients with glaucoma simplex became so artificially myopic from ciliary spasm induced by D.F.P. that the resultant vision was unsatisfactory. For example, one of these patients had 20/20 corrected vision prior to the instillation of D.F.P. While receiving D.F.P. (1 drop of 0.05-percent solution, twice daily) in the left eye, her vision varied on different visits to the clinic from 20/50 to 20/100. A manifest refraction on a day in which the vision was 20/70 showed that a −2.5D. sph. lens was required to give 20/20 vision. Because of the variability of the ciliary spasm in this case,

the induced myopia could not be satisfactorily corrected by a permanent change in the spectacle lens. In three of the four eyes with chronic congestive glaucoma, the anterior chamber became more shallow after the use of D.F.P., without any reduction in tension. A reduction in depth of the anterior chamber was also noticed in several eyes with glaucoma simplex.

Advantages of therapy

The advantages reported for D.F.P., when it satisfactorily controls the tension, are the convenient infrequency of administration and the absence of a local sensitivity reaction. The advantage of fewer daily instillations is somewhat offset by the pain which may occur and the temporary myopia which may result. One case treated with D.F.P. but not included in this series is of especial interest. In this patient, the use of D.F.P. apparently caused a ciliary spasm so severe that the resultant traction on the choroid and retina produced a retinal detachment.

Report of a case

A 62-year-old white man, with moderate myopia corrected to 20/30 in both eyes, had glaucoma simplex, and the tension was satisfactorily controlled on pilocarpine (3 times daily) ordered by his local ophthalmologist. Because of the inconvenience of the mid-day dose, it was decided to try D.F.P. Two drops of a 0.1-percent D.F.P. were placed in each eye and immediately following the instillation severe pain developed in both eyes and vision became blurred. These symptoms disappeared after 24 hours. The following morning (approximately 36 hours after the instillation of the D.F.P.) the patient noticed a grayish veil hanging down nasally in the visual field of the right eye. Metamorphopsia developed and the upper field became distorted. One month later when the pupil was dilated for the first time, the lower retina was found to be detached. The patient was then referred to the Wilmer Institute. On examination, a disinsertion of the retina in the lower temporal quadrant with detachment of the lower retina was found.

Conclusion

From our studies on chronic glaucoma, it would appear that when other miotics such as pilocarpine, eserine, and especially furmethide fail to control the tension, D.F.P. in the concentrations used has little chance of success. Furthermore, although D.F.P.* may be ineffectual, it is not always innocuous.

Johns Hopkins Hospital (5).

* The D.F.P. used in this study was supplied by Dr. A. M. Harvey, Dr. J. L. Lilienthal, Jr., and Dr. D. Grob of the Department of Medicine, Johns Hopkins Hospital, to whom the author expresses his thanks.

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NOTES, CASES, INSTRUMENTS

METASTATIC FUSOSPIROCHETAL ABSCESS OF THE ORBIT*

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Metastatic abscess of the orbit is not uncommon and orbital abscess caused by Borrelia vincentii and Fusiformis dentium is not rare, but the combination of the two is an unusual occurrence. In most instances the latter condition is the result of the extension to the orbit of an infection of the maxillary sinus following a dental infection. Dunnington and Khorazo,[3] in 1936, reported a survey of the literature and found only 13 cases of ocular infection due to Borrelia vincentii and Fusiformis dentium. Walker[4] reported a case of abscess of the orbit and suppurative panophthalmitis produced by these organisms as the result of an infection of the maxillary sinus following the extraction of a tooth. Burch[2] reported a case of metastatic orbital infection from a staphylococcic pulmonary infection. Berens[1] stated that metastatic abscess of the orbit occasionally arises in infectious diseases, scarlet fever, chicken pox, and influenza, and from surgical operations for infections in other parts of the body, as pelvic cellulitis and uterine disease. Because of the rarity of the condition, it is believed that the following case is worth reporting.

CASE REPORT

R. M. C., a white man, aged 52 years, was admitted to this hospital on October 10, 1944, for the treatment of bronchiectasis, severe, bilateral. The pulmonary condition was too extensive for surgery and his therapy consisted of postural drainage and frequent bronchoscopies with the insufflation of sulfonamides into the bronchial tree. Sputum examination yielded Gram-negative fusiform bacilli and spirilla on smear.

On January 14, 1946, he complained of pain in the right eye. Examination revealed slight puffiness of the right lower eyelid, but intraocular examination was negative. Heat was applied, and two days later the swelling had increased and it was noted that ocular motion was limited.

On January 16, 1946, an abscess on the outer aspect of the left arm was incised. Purulent material was found which had a very acrid odor and was rather viscous and gray in appearance. Smears of this material revealed many spirilla and Gram-negative fusiform bacilli, but there was no growth on culture. By the following day, there was marked swelling of the right lower eyelid and fluctuation could be felt. The conjunctiva was markedly injected and the globe was proptosed about 6 mm. and fixed. A 22-gauge needle was introduced in the area of fluctuation and pus was encountered at a depth of 3 cm. Aspiration yielded 4 cc. of thick, creamy, purulent material with a foul acrid odor. An incision was made along the needle to the abscess cavity and a drain inserted. Smears of this material were found to contain bipolar staining bacilli, Gram-positive cocci in chains, and spirilla. No growth was obtained on culture. The abcess was irrigated frequently with 20,000 units of penicillin in 2 cc. of normal saline and within a week had completely healed. The proptosis subsided rapidly, but some

* From the Veterans Administration Hospital. Published with the permission of the chief medical director, Veterans Administration, who assumes no responsibility for the opinions expressed or the conclusions drawn by the author.

limitation of motion of the globe persisted for several months.

On January 28, 1946, an abscess on the anteromedial aspect of the left thigh was incised with the finding of purulent material similar to that above. During this time a series of daily blood cultures for five days was reported as sterile after two weeks' incubation.

SUMMARY

A case of metastatic abscess of the orbit, accompanied by metastatic abscesses in other parts of the body due to Borrelia vincentii and Fusiformis dentium infection of bronchiectasis, has been reported.

Veterans Administration Hospital.

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TECHNIQUE OF CATARACT OPERATION WITH THE ORAL-SUCTION CUPPING APPARATUS*

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Intracapsular extraction of the lens by means of suction in operations for cataract is an already known and approved method. It is the purpose of this paper to present an improved cupping apparatus and the technique of its use in order to acquaint ophthalmologists with a method of cataract extraction which is at once simple and safe.

Although it is not the aim of this paper to discuss the various techniques of cataract extraction, it would be well to refer to some of the fundamental principles upon which all these techniques are based. Among these are: (1) Complete anesthesia and akinesia of the eye. (2) Corneoscleral sutures complete with a conjunctival flap. (3) Peripheral iridectomy. (4) Intracapsular extraction of the lens.

It is the purpose of this paper to demonstrate that, no matter what kind of cataract is being operated, the cupping apparatus under discussion is the ideal instrument to use to extract the lens itself. Simple to apply, its handling is easy and delicate. Since there is automatic control of vacuum, the surgeon is able to do his task with a feeling of security. Assuring a precise apprehension at a chosen point, it permits an almost nontraumatic rupture of the zonule. The nucleus turns within its own capsule so that its posterior surface becomes the anterior one when passing through the corneoscleral incision.

DESCRIPTION OF APPARATUS

The apparatus is made up of four parts: (1) The nozzle (the cupping part, itself) which is made of chrome-plated metal. This concha-shaped nozzle is one of the principal innovations of the instrument. (2) A chrome-plated metal tubular body. (3) A tube made of rubber. (4) A mouthpiece.

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* Report presented to the V. Brazilian Congress of Ophthalmology, Salvador, Brazil, 1945.

As its name implies, the mouthpiece (fig. 1, no. 1) is held in the mouth, between both lips, in such a manner that suction is produced by the mouth muscles only. In this manner, the vacuum is regulated. The mouthpiece, 22 mm. in length, is made of an acrylic material and is easily sterilized in steam (autoclave or sterilizer). It cannot, however, be sterilized by certain solvents, such as chloroform, various organic acids, and so forth.

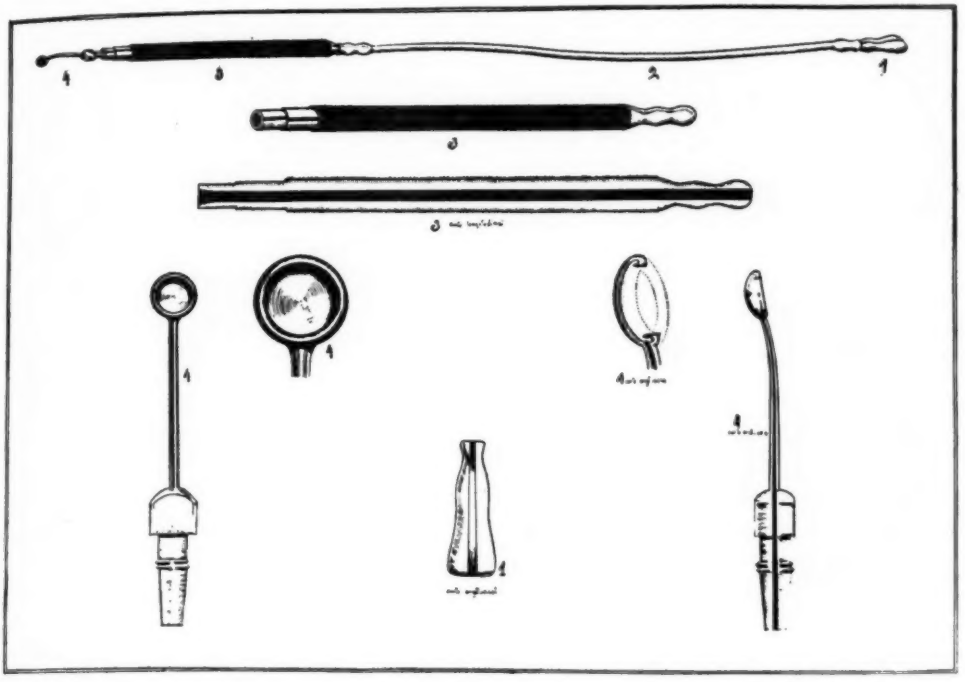

Fig. 1 (Falcão). Cupping apparatus for cataract operations (top) ready for use, and its separate parts: 1, mouth piece; 2, tube; 3, body; 4, nozzle.

The rubber tube (fig. 1, no. 2) is able to withstand a pressure of 90 cm. Hg. Its average length is 40 cm.; its diameter, 1.5 mm.; its circumference, 3.5 mm. It is designed to link the mouthpiece with the body of the apparatus.

The body (fig. 1, no. 3) is a hollow, chrome-plated metal cylinder, 12.5 cm. in length. Its circumference is 8 mm. Simple in construction and like a pencil, the body portion of the apparatus is strong but light so that it can be handled with ease and can be made to follow every movement of rotation with dexterity. The rubber tubing is fitted to one end. At the other end is a polished conic joint. The nozzle, maintained in position by a delicate thread, is attached to this conic joint. The body can be sterilized by steam or hot air, as well as by certain chemicals such as formalin.

The nozzle (fig. 1, no. 4) is a small and thin chrome-plated metal tube. At one end is the trunk which fits the conical joint of the body. As has been mentioned, a thin thread fixes the nozzle on the joint and makes the connection airtight. A careful test must be made to see that an airtight connection has been achieved.

At the other end of the nozzle is the concha which, when introduced into the

anterior chamber in juxtaposition with the anterior lens capsule, grasps the cataract. The nozzle can be sterilized with either steam or hot air.

Nozzles of two sizes accompany this apparatus. The smaller one (diameter, 2.4 mm., circumference, 3.4 mm., depth, 1.7 mm.) is designed to extract the lens without turning it to 180 degrees. The larger nozzle has a diameter of 3.4 mm., a circumference of 4.6 mm., and a depth of 1.7 mm. It was designed for use in the operating of hypermature cataracts with large, hard nuclei. The technique of lens extraction with this nozzle is similar to that employed in the use of several well-known cupping apparatuses. A rotating movement of 180 degrees is used to extract the lens with the capsule and nucleus intact.

The innovation peculiar to these nozzles is the shape of the concha. In spite of its small size (its diameter is less than the length of the jaws of Arruga's capsule forceps), the concha has a large gripping capacity. The circular edge of the concha has no abrupt angles (fig. 1, no. 4). Its somewhat concave shape gives it an area of sufficient size to permit it to adhere no matter from what angle the manipulations are performed.

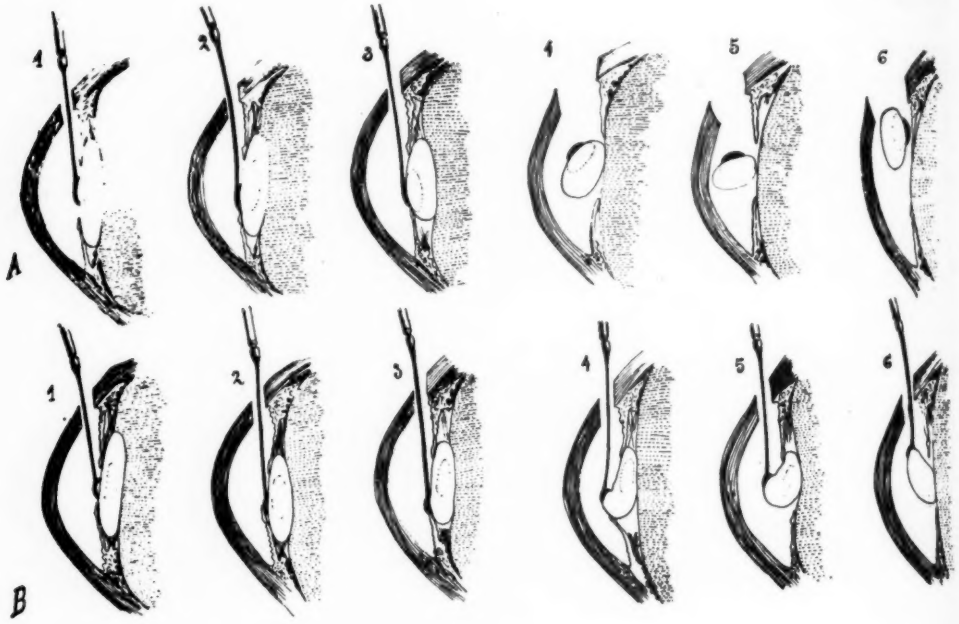

Fig. 2 (Falcão). Technique of grasping and extracting the lens with (A) the larger cupping apparatus and (B) the smaller cupping apparatus. (Author's note: In order to make the subject matter more clear, the above drawings do not keep the precise anatomic relation.)

Technique of operation

Although the management of the cupping apparatus is simple, its operation requires extreme care and delicacy. It is also essential that illumination be adequate and correct.

Use of smaller nozzle. Assemble the various parts of the apparatus and check to see that they are in perfect working order. With the eye under proper mydriasis, the cupping apparatus is introduced, preferably through the temporal side of

the wound. It is passed down over the iris close to the inferior edge of the lens, and the concha is gently applied to the anterior capsule.

When the proper moment for grasping the lens has arrived, vacuum is created by suction on the mouthpiece of the apparatus. The operator devotes his attention to rupturing the zonule and the hyaloid-capsular ligaments. He can increase or decrease the suction. The maneuver of detaching the lens is identical to that employed with forceps. All that is needed is to raise and gently withdraw the nozzle and lens. If necessary, a circular tenaculum or a stilet may be used below the place of zonular adherence to complete the rupture of the crystalline ligament.

Use of large nozzle. In general, the technique employed with the larger nozzle is the same. There must be sufficient mydriasis to permit the adjustment of the concha somewhat below the horizontal meridian of the lens. After the zonule has been ruptured, a movement of rotation is set up at the same time that the cupping apparatus is lifted and withdrawn. The nucleus and its capsule come out adhering to the concha.

It is important to remember that, during the use of the cupping apparatus, the power of adhesion is always increased when traction is exerted in a direction perpendicular to the plane at which the concha adheres to the surface.

Discussion

Since the extraction of the lens has, throughout all the periods of cataract operation, been a most delicate and difficult problem, any technique which facilitates its removal and prevents accidents must be considered an improvement. My aim, therefore, has been to simplify to the utmost techniques already in existence. Mathieu, in 1866, and Hertz of Vienna, at a later date, removed cataracts by suction, but their methods did not improve upon the then prevailing techniques.

As time went on, vacuum in the cupping apparatus was obtained by means of pneumatic pumps of various types. Evolution of the devices progressed from the pear of Stoewer through the more modern electrical machines of Barraquer and Castroviejo to the fountain pumps of Dimitri, Rochon-Duvigueand, Arruga, and so forth. Fisher, of Chicago, decided to insert a diverticulum in the connection tube between the pumping engine (1/6 h.p.) and the cupping apparatus itself. His diverticulum is of rubber and has a mouthpiece by means of which the vacuum is regulated. This does not, however, afford an entirely satisfactory means of regulation.

After giving fair trial to these various types of cupping apparatus, I concluded that to be truly satisfactory the apparatus should have these features: (1) Perfect vacuum, perfectly regulated. (2) A nozzle sufficiently small to permit insertion through half-dilated pupils. With the cooperation of Dr. Cintra do Prado, professor of physics at the Polytechnic School in São Paulo, and his assistants, experiments for improving existing apparatus were undertaken.

By means of the mercury vacuum meter, temperature 24°C., corrected pressure 700 gm., we calculated that the oral vacuum produced by the mouth muscles oscillates between 350 to 450 mm. The highest vacuum obtained was 635 mm., exactly the amount produced by the pump of Barraquer. This eliminated the criticism that orally produced vacuum would be insufficient to permit the proper application of the cupping apparatus.

The grasping power of the cupping apparatus does not, however, depend entirely upon the production of a vacuum.

Earlier failures did not depend upon the lack of sufficient suction power, alone. The structure of the nozzle by means of which the lens is grasped was also at fault. I felt that the area which would adhere to the crystalline lens could be increased, and that better adhesion could be achieved.

To substantiate this theory an interesting experiment was devised. A small ball made of thin rubber was filled with water and placed on a coin balance. The liquid tension inside of the ball was similar to that of a swelling cataract, and the ball was stout enough to support a traction force greater than any crystalline lens could endure without breaking up.

The nozzle of the cupping apparatus was adjusted to this ball, vacuum was created, the ball was drawn slowly and progressively toward the scale of the balance, and its weight in grams was noted at the precise moment of its liberation. Following this plan, the efficiency of a number of different types of cupping apparatuses, in which the suction pressure registered from 200 to 700 mm. Hg, was measured. The results showed that the only cupping apparatus approaching ours in efficiency was that of Barraquer and of Rochon-Duvigueand. The results for our apparatus showed:

Vacuum	*Small Nozzle* (2.4 mm.)	*Large Nozzle* (3.4 mm.)
700 mm.	60 gm.	95 gm.
400 mm.	35 gm.	55 gm.

After testing the same cupping apparatus several times, employing strong oral aspiration, we recorded these results: Oral suction using small nozzle measured 45 gm.; using large nozzle, 85 gm.

Since the normal lens weighs between 0.20 and 0.30 gm., we concluded that our cupping apparatus was capable of lifting 200 to 400 times the weight of a normal lens. This would be more than the power needed to rupture the zonule and to extract the lens.

After the results of these preliminary experiments were corroborated by work done on the eyes of animals, we operated on 12 patients from the clinic with this apparatus. Eleven of these operations were successful. The 12th case, that of a boy, aged 16 years, failed because of the unbreakable resistance of Zinn's ligament.

Summary

A cupping apparatus constructed on the principle of oral suction is presented. The mouth muscles are used to produce sufficient vacuum, and respiration is not disturbed. Between 350 and 450 mm. Hg pressure is required to extract the lens, and this amount of pressure can be regulated automatically. The apparatus is equipped with a smaller and a larger nozzle. Either size can be used with equal ease; the smaller is designed for extracting the lens without turning it to 180 degrees; the larger is to be used when a rotating movement of 180 degrees is required. The simplicity and security offered by the technique of this method of intracapsular cataract extraction recommend its use.

Rua Visconde de Inhaúma—59.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

December 19, 1946

DR. BURTON CHANCE, *chairman*

PATHOGENICITY OF DIPHTHEROIDS ISOLATED FROM HUMAN CONJUNCTIVA*

DR. CHARLES WEISS,† and MR. M. C. SHEVKY,‡ presented this subject. Diphtheroids, resembling *C. xerose* and isolated from the human conjunctiva grow well in a menstruum of mucin. Similarly, when suspended in this medium and inoculated into the anterior chamber of the eyes of albino rabbits, cultures retain their viability for several days, although they are rapidly destroyed in salt solution.

Intraocular injections of rabbits with diphtheroids, suspended in saline, produce moderate inflammation of the ciliary process. When suspended in mucin, the reaction lasts longer, is much more severe, and is associated with an acute keratitis. The lesions usually regress spontaneously within 2 or 3 weeks.

When killed cultures of diphtheroids in saline produce mild inflammatory changes in the ciliary process which can be seen in histologic sections; none are visible grossly. In a menstruum of mucin, the inflammatory reaction is more severe. Since mucin by itself is relatively innocuous, it is suggested on the basis of these studies and those of others that it protects bacteria from the digestive action of humoral and cellular proteolytic enzymes and other immunologic defense mechanisms. Living diphtheroids are thus permitted to grow and exert their pathogenic activity.

By means of the recently developed methods of Muller and Miller and Pappenheimer and Johnson, it was possible to demonstrate that when diphtheroids are grown in a medium of very low iron concentration, they yield a toxic filtrate which is injurious to the uvea and cornea but not to the skin or conjunctiva of albino rabbits.

Studies which had been planned on the specific chemotherapy and serotherapy of diphtheroids were interrupted because of the war emergency.

On the basis of these investigations, it may be concluded that diphtheroids which are present on the normal or the inflamed conjunctiva may be considered as potential pathogens which can exert serious injury when they find their way into the interior of the eye.

Discussion. Dr. Luther Kauffman: I wonder, from a practical point of view, in treating conditions involving the conjunctiva whether the proper procedure would be to get rid of the mucin. I am reminded of the solution of monohydrated sodium carbonate, which Dr. Lehrfeld presented before this section some years ago in his treatment of vernal conjunctivitis. It would also be interesting to ask Dr. Weiss if he knows whether other bacteria receive the same protective help from mucin as these diphtheroids do.

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* From the Laboratory for Ophthalmic Research, Mt. Zion Hospital, San Francisco, California. Aided by a grant from the Columbia Foundation.

† Present address: Laboratories of the Jewish Hospital, Philadelphia 41, Pennsylvania.

‡ Now at the University of California, Department of Bacteriology.

Dr. Burton Chance: The early death of diphtheroids reminds me of my own experience in the early days of my medical practice, when diphtheria was a frequent disease. For two winters I volunteered at the old Municipal Hospital. In one week, 275 sick persons were inspected. There were a good many patients there because the bacteriologist, who was at the summit of bacteriology at that time, had found what he believed to be the diphtheric organism in the conjunctiva and fauces. A few days after the children were admitted, another examination was made, with negative results, which created more than a headache, both on the outside and inside the hospital. The children were interested to know whether or not it had been true. The people outside were kicking because their children had been taken away from home and isolated. Having to have their own toothbrush and to carry out other hygienic measures were the sources of complaints from the children. Also, there were no signs of the old diphtheria of the conjunctival tissues that prevailed in earlier times. My teachers would refuse to accept a diagnosis of diphtheria unless there were actual structural and infiltration changes. Your statement concerning the evanescence of the diphtheroids, therefore, has reminded me of that somewhat confusing experience.

Dr. Charles Weiss, in closing, replied to the first question: Generally speaking, mucin on the inflamed conjunctiva is due to bacteria. Of course, it may also be due to chemical irritants. It seems reasonable, on the basis of our work, to remove it.

I mentioned in the course of my presentation that the virulence of a number of other bacteria is increased by mucin. Among them are: the meningococcus, the gonococcus, V. cholerae, and also the virus of influenza.

Experience in testing those with defective color sense

Dr. Burton Chance stated that from his earliest years, even in his first school days, he became aware that some persons were color blind, and ever since then he has been interested in color. In recent years, that visual defect has become the subject of so much investigation that he has ventured to tell something of his own interest in it and to express his beliefs concerning it.

The perception of color by human beings is an intellectual process involving psychologic and physiologic factors operating with the effects of light upon the chemical elements in the retina. The average person is able to distinguish all seven colors in the visible spectrum, and it is not improbable that animals and birds perceive beyond what mankind can define. There occasionally is found one whose appreciable "spectrum" is shortened at either end, if not both ends. For others, the ends are only more or less indistinct. In certain persons, however, the extent of the spectrum is not present; hence the appellation—color blind. A better and more kindly term is achromatopsia. Men more than women are affected. It is hereditarily transmitted from one generation to another through females who might not themselves be known to be affected. In pure cases, the eyes are not visibly changed structurally. Disease of the retinochoroid may be accompanied by defect in color perception. The color manifestations of the defect are, however, not usually comparable to those of the congenitally deficient. A singular anomaly is shown by those who have a unilateral deficiency; that is, complete perception is possible with one eye.

The measurement of color perception has aroused serious consideration in the

arts and in transportation, as well as in the definition of members of the military forces. Many notable persons in history have been found deficient and, since it was a pronounced defect in the case of John Dalton, the famous English physicist, it has been given deep study and various schemes for testing have been devised.

Such tests have been composed of wools, colored charts, and colored lights which are compared or matched with certain standard colors selected after prolonged investigation. In practice, red and green have been the colors most frequently found deficient; hence, these colors have been adopted as the basic standard for all tests.

Color perception is an unsolved mystery. Many theories have been proposed, but none solves all the problems, although the advocates of each theory defend their hypotheses violently. Thus far, the theory offered by Thomas Young and later similarly arrived at by Helmholtz has the least uncertainties. According to Young and Helmholtz, each color excites its own system of nervous conduction to the brain's perceptions.

Being a congenital defect, color blindness cannot be cured or even reduced—all schemes proposed are only false promises. Individuals can be trained to distinguish more fully one color from another; yet, when standard lights or plates are modified, as by foggy atmosphere or color dilutions, the natural defects become manifest.

All subjects do not have identical defects—some lack one or two; others more, even all seven colors. Observers have, therefore, classified them according to the number. Some persons showing only a lessening of the color strength are classed as anomalous of those color classes. Increasing attention to the "anomalous" is being carried on today. Those persons to whom all colored objects appear to be black are spoken of as the monochromatic. Despite all the interest shown in the past 50 years, no new fundamental facts relating to the problem have been solved; their solution rests with the photochemistry of the retina.

Discussion. Dr. George F. J. Kelly: It is my impression that you spoke of several cases of normal color perception in one eye and abnormal color perception in the fellow eye. Was there any evidence of pathologic changes in the fundi of the abnormal eyes?

Dr. P. Robb McDonald: I have been interested in Dr. Chance's paper because, for part of the time that I was in the Service, I was working with those who were engaged in developing tests for color vision.

As Dr. Chance has said this is a rather confusing subject. I notice that he also stuck to the term "color defective." This is a much more appropriate term than color blind. There are a lot of people who have defective color vision but who are by no means color blind.

In setting up tests for color vision, there were certain facts that had to be known. They were essentially:

1. A "job analysis" to determine what color discriminations were actually required of pilots, bombardiers, air crew, and so forth.
2. An evaluation of the tests of color vision that were available.
3. The development of new tests.
4. The reproducibility, reliability, and validation of the tests that were adopted.

The problem of landing a plane in the daytime was not too difficult because usually other clues than color were employed to determine whether one was about to land on tilled or flat surfaces. At night the problem was more difficult. The

runway markers might be colored lights of low intensity, the landing might be made with glide-path indicators, or the only communication between the tower and the pilot might be by a directional light such as the "biscuit gun." Those who worked about the airplane also had to make certain color discriminations. The wiring was usually coded by color, the various fuses had color codes, and so forth.

What everyone wanted was a quantitative test of color vision. One of the closest approaches to this was a lantern developed by Dr. Louise L. Sloan. The test was modified from one developed by the R.C.A.F., which in turn was a modification of the Williams lantern. The test was called a color-threshold test, and consisted of presenting eight different colored lights at eight different intensities of illumination. The minimum intensity was that at which most normal individuals called the color correctly. A score of 62 to 64 was considered normal.

We were fortunate in having a considerable number of color-defective individuals at Randolph Field, and Dr. Sloan was able to test them on the various tests of color vision. In all, about six tests were used—the Ishihara, the American Optical Company's pseudo-isochromatic plates, an abridged edition of the same, the Rabkin polychromatic plates, an anomalscope test, and the color-threshold test. Several other tests were employed at one time or another. Either before or after this battery of tests, the individuals were given "practical" tests; that is, the identification of colored flares actually fired from an airplane, the identification of colored signal lights, the identification of colored codes on wires, and so forth.

On the basis of these tests, the color-threshold tester was the closest approximation to a quantitative test. I think that in the future we may have two types of color-vision tests. One that we can do in the office to determine whether an individual is normal or not, and one which the military can use to determine whether a soldier is color safe or not.

Dr. Burton Chance, in closing: In the several instances where I have seen perfection in one eye but defective perception in the other, there were no visible changes in the fundus. It is more than likely that if it be true that the perception of color is generated by the action of light on the retinal pigment, there was something constitutionally lacking in such eyes as gave rise to the defect. Therefore, in this consideration, I would not class a unilateral case presenting changes in the fundus as a true case of color blindness.

I wish to thank you, Dr. McDonald, for telling us something of what was done in the last Army. I regret that I was afforded no opportunity to witness such studies personally.

George F. J. Kelly,
Clerk.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

January 15, 1947

Dr. Howard F. Hill, *presiding*

Complications encountered in keratoplasty

Dr. R. Townley Paton of New York introduced his subject with a discussion of essential preliminary considerations. Only homotransplants or autotransplants have proved successful. Of the four types of corneal transplants—(1) total corneal transplantation; (2) total lamella transplantation; (3) partial lamella transplantation; and (4) partial penetrating corneal transplantation—the last method

gives the best results in specially selected cases. He classified cases for operation as: (1) For cosmetic improvement alone; (2) favorable for improvement of vision; (3) partially favorable for improvement of vision; (4) unfavorable for improvement of vision; (5) for treatment of descemetocele.

The most favorable cases are those in which there is a nebulous type of opacity, quite central, and in an otherwise normal eye. There must be no active corneal disease present, or active infection of the conjunctiva, sclera, or uveal tract. There must be no increased intraocular pressure and no vascularization of the cornea. Blood staining of the cornea and conical cornea usually indicate favorable cases. The partially favorable cases are those in which there is some vascularization present and in which the opacity is dense with little clear cornea surrounding it, cases of adherent leukoma, shallow anterior chamber, and some cases of corneal dystrophy. Aphakic eyes, as a rule, do not do well, but some good results have been obtained. Cases in which the scarring is not too dense but in which there is a marked reduction in the corneal reflex should be given a guarded prognosis. Unfavorable cases include most forms of dystrophy, most forms of lipoid and calcareous dystrophy, trachoma where there is a dense vascularization, lime burns and powder burns, hyperirritable eyes in which the cornea is densely and completely scarred as the result of acid and gas burns, pemphigus, and cases of severe symblepharon.

Dr. Paton stressed that, no surgeon, no matter how well qualified, should attempt this operation before experimenting on animals and dead human eyes and refreshing his memory on the anatomy and physiology of the cornea.

The selection, obtaining, and preserving of donor material was briefly discussed. Types of operation are: (1) Use of stencils; (2) double-bladed knife or square window; (3) the trephine or round window. The technique of these procedures was summarized. He feels that the trephine method is the most advantageous because: (1) Better cosmetic result is obtained. (2) It is easier to complete the cutting of the window with scissors. (3) There is less danger of dulling the edge of the instrument in sterilization because of the adjustable collar. (4) An outline is made more easily with no danger of perforation because of the adjustable stop. (5) The donor window can be cut completely, thus eliminating the use of scissors.

Dr. Paton also prefers to use two sutures of different color because: (1) This gives increased ease of tightening; (2) more even distribution of pressure can be obtained, especially when there is a tendency toward overriding of one side of graft; (3) there is less danger of complication if one suture becomes frayed or is accidentally cut; (4) if further reenforcement is desired before the ends are cut, the suture can be anchored diagonally opposite in the episclera near the limbus or in the corneal tissue at the limbus.

Several points of consideration at time of operation were noted. Eyes with nystagmus may be operated upon, but the results are not good, as these eyes are invariably amblyopic. Cataract extraction and squint operations should be done after and not before the transplant has been performed. In aphakic eyes, the sword knife or the Filatov prophylactic spatula should be used to hold back vitreous during operative procedures. Operations on children before the age of 8 or 9 years or on glaucomatous eyes, should be avoided.

The postoperative complications may be grouped as follows: (1) Those produced by poor technique and unsatis-

factory instruments may result in: (a) edema of graft, (b) poor fit which may also cause the anterior chamber to collapse, (c) anterior synechias which often cause clouding of the graft. (2) Those that result from poor choice of patient. (3) Poor donor material and vascularization. (4) Unforeseen complications, such as infections and stitch abscess. (5) Cataract. (6) Glaucoma.

In summarizing the results, Dr. Paton said that in favorable cases visual improvement from 20/200 to 20/15 may be expected, but the latter acuity is rarer, occurring in about 2 percent of cases. Most cases require, postoperatively, a high minus correction with a high cylinder correction. Conical cornea cases give favorable results, but should not be operated upon unless contact glasses are not well tolerated, or if visual improvement cannot be obtained further than 20/200. A large graft should be used in these cases whenever possible.

Discussion. Dr. Brendan Leahey in discussing Dr. Paton's paper, said that much more keratoplasty has been done in New York than in Boston, and that, in the 8½ years since he obtained his first clear graft, his own series had risen only to 40 cases. Despite this, however, he felt sure he could at least hold his own with Dr. Paton when it comes to complications. He had hoped that Dr. Paton would say more about the removal of blood vessels, as that has been one of his worst problems in getting cases ready for operation. Some of the vessels can be closed by means of cautery or diathermy applied to the vessel trunks at the limbus for 2 mm. He has done a very large number of these and, in general, his results were unsatisfactory. About 80 percent of the vessels soon reopen. Stripping is helpful when the vessels are large and superficial. He has done relatively few of these, but again, results of stripping alone are disappointing. Radiation is the most effective method when combined with stripping or peritomy.

The radiation can be either X ray or radium. The effect is identical, if filters are used to get the same rays through. Radiation, however, works only on tiny vessels and new capillaries, so the larger trunks require the other methods.

The more popular method at present is to use Beta radiation by means of radon or radium in a special small pencil-like applicator as designed by Dr. Burnam at Johns Hopkins. With very slight care this can be applied by the ophthalmologist himself to the blood vessels for the requisite number of gram seconds.

Dr. Paton spoke of accidentally cutting sutures. It is disconcerting but not serious when one is occasionally cut. The cut suture may be pulled through and rearranged so that an extra knot can be tied. If this is impossible, a new suture can be inserted in the same holes or new ones, even though the eyeball is open, by using a little needle counter-pressure instrument. This instrument has two little pronged feet that stick against the cornea. The needle can be pushed between these feet without much trauma to the cornea. This instrument is also handy for repairing traumatic corneal or scleral wounds.

Among the postoperative complications, anterior synechia has been the most common in his experience. A slight anterior synechia at the edge of a clear graft is almost certain to cause clouding of the graft in a few months. It may cause proliferation of connective tissue on the back of the graft, or it may cause a haziness to the stroma and edema of the epithelium like dystrophy. There is also, of course, the danger of glaucoma.

If these synechias are freed through a small limbal incision without iridectomy, there are usually new anterior synechias created near the limbus. Dr. Leahey has freed anterior synechias on three of these cases (and also on some cataracts with

beginning edema of the cornea at the site of adherent iris pillars) by a simple and effective procedure. A scleral incision is made as for a cyclodialysis, but located only about 3 mm. outside of the limbus. The iris repositor is slid into the anterior chamber and the synechias swept away.

Proliferation of connective tissue on the back of the graft is not uncommon. It is practically sure to occur in the presence of anterior synechias. In other cases it grows in from fibroblastic tissue at the margin of a perfect graft. We have no treatment for this, as radiation here is not considered effective. Fortunately many cases may proliferate in only 1 mm. or so and then stop just about the time we are really getting worried.

Edema of the graft is another untreatable complication—provided it is not the result of anterior synechias or glaucoma. It may remain after operation; or some cases may be clear for 6 to 10 months, then suddenly develop slight edema of the graft and remain that way. Hypertonic saline or glycerine and vitamins seem to make no difference. One of the reasons for this edema is excessively dense scar tissue around the graft so that it has defective nutrition.

A minor complication which Dr. Leahey often finds is a large astigmatic error. He has a number of cases in which vision is near normal with cylinders of between 2 and 7 diopters. In one recent case having both a transplant and a cataract extraction, vision was improved to 20/30 and J1 with a: +4.00D. sph. ⌒ − 12D. cyl. Vision in these cases could be improved to 20/20 with contact lenses. Although he is doing a lot of contact-lens work, he has not yet prescribed one for a transplant case. Incidentally, in cases such as this, in which, both the cataract and the transplant are necessary, the transplant should always be done first and the cataract extraction second.

In closing, Dr. Leahey said that although the unpleasant features of this operation have been presented, he is very enthusiastic about the results of this procedure and that, in case of need, he would not hesitate to recommend the operation to a member of his own family or to submit to it himself. He added that in this event he would be glad if Dr. Paton were the surgeon working on him.

Dr. Edwin Dunphy then spoke of the organization of the Eye-Bank in Boston as a branch of the Eye-Bank in New York. On Dr. Dunphy's request, Dr. Paton discussed the organization and operation of the New York Eye-Bank, stressing the need of the material not only for keratoplasty, but also for research.

Mahlon T. Easton,
Reporter.

SOCIEDAD OFTALMOLOGICA DE MADRID

January 17, 1947

Suprasellar choristoma

Dr. Obrador, Dr. Bartolozzi and Dr. Carreras Matas presented a patient in whom the ophthalmic examination disclosed bilateral papillary atrophy, with total loss of vision in the left eye and a scotoma in the upper temporal quadrant of the right eye. The diagnosis was a probable suprasellar tumor. Dr. Obrador operated and removed a tumor which was situated between the optic nerves in front of the chiasm. The anatomic-pathologic examination showed that it was a choristoma. A few days after the operation the visual field of the right eye was considerably improved, and the acuity of this eye rose from 3/50 to 9/10.

Discussion. Dr. Marin Amat: This morning I saw the patient in my ophthalmologic service in the Provincial Hospital and could see total atrophy of the papilla of the left eye and partial atrophy of the

papilla of the right eye; but since in the latter eye the atrophy had all the characteristics of a postneuritic atrophy (thickened contour of the papilla, thin arteries), I wonder if in the beginning, before being operated, it might have been treated as a case of Foster-Kennedy Syndrome. The result is clear, the finding and the extirpation of the tumor.

Professor Carreras. The case which has just been discussed by Dr. Bartolozzi and Dr. Carreras Matas, as ophthalmologists, and by Dr. Obrador, as a neurosurgeon, shows how necessary it is to have the collaboration of the ophthalmologist, the internist, and the neurosurgeon in order to treat with the greatest degree of skill a clinical case which is more or less complicated and which none of the specialists working alone could have solved satisfactorily. The fact that this patient shows complete amaurosis of one eye with complete optic atrophy; and, in the other eye, incomplete optic atrophy, with a visual-field defect of a complete upper temporal and part of a lower temporal sector, the vertex of the sector reaching onto the fixation point, makes me diagnose the case as one of an intracranial lesion (probably a tumor) which started in the chiasmal region and which extended mainly toward the left side interfering with most of the crossed fibers from the right side and all the fibers (crossed and uncrossed) of the left optic nerve. My diagnosis is supported by the fact that the X-ray studies show the sella turcica to be apparently normal.

Conjunctival cover for injury

Dr. Mario Estaban showed a case of a penetrating injury to the eye. There was a scleral tear of about 7 mm. at the edge of which vitreous began to appear. His first thought was to enucleate the eye; however, he limited himself to the use of a conjunctival cover The eye recovered and has vision of 2/3.

In ocular traumas we shall be better surgeons if we do fewer enucleations. It is necessary to adopt a conservative attitude when there is something which can be saved.

Repair of a scleral wound can be made either by closing the edges or by using a covering of conjunctiva. A good method of treating the edges directly is to use a double-armed suture which brings the edges of the sclera and conjunctiva together at the same time. There is, however, the disadvantage that one has to exert pressure on the globe in order to force the needle through the fibrous tissue of the sclera.

A conjunctival covering, on the other hand, can be made easily and without pressure. One good method is to detach the conjunctiva at one of its edges and bring a small strip over to the opposite side so that when the suture is made the conjunctiva slides over the scleral wound and keeps it covered.

Discussion. Dr. Carreras said that he agreed with Dr. Mario Estaban that one should not be hasty to enucleate an eye which is seriously injured, although the chances of saving it may be small. Some 21 years ago he published a paper, describing the case of a patient who, during a wild carnival frolic, had a lemon thrown in his face with such force that it broke the lens in front of his left eye and caused the temples of the frame to cut the eye, causing a wound which took in the whole vertical meridian of the cornea and included some 5 mm. of the sclera. There was a hernia of the iris and of the ciliary body, and vitreous appeared at the edges of the wound. The patient was rushed to a first-aid station, where the doctor did nothing but put a sterile pad on the eyes and advise that he be taken to an ophthalmologist for removal of the eye. Operating on him the same night, I reduced the hernia of the iris, sutured the cornea and the sclerotic, and then made a conjuncti-

val covering. After a binocular bandage had been applied, the patient was put to bed and protein therapy was started. The result was that the eye was cured. Final vision was 2/3, and a myopia of 3 diopters, which the patient had had before the accident disappeared. The lineal cicatrix of the cornea is hardly visible.

Dr. Mario Estaban answered Dr. Carreras, thanking him for his discussion which supported his conservative procedure.

Ophthalmologist and Cranial Surgery

Dr. Mario Estaban read a paper on "The Collaboration of the Ophthalmologist in Cranial Surgery in War."

War wounds produce a large number of serious cranial lesions in which it is rare not to find the ocular system more or less affected. The collaboration of the ophthalmologist and the surgeon is always effective and often indispensable for diagnosis, in treatment, and during the progress and postoperative course of cranial injuries. In diagnosis, the ophthalmologist can outline the difficult types of vascular lesions, oculomotor lesions, and lesions of the optic pathways and give their topography. This will enable the surgeon to fix accurately the indications and localization of the operative procedure.

In treatment, the surgeon and the ophthalmologist can work together in a great many cases in which there are many wounds and mixed lesions of the cranium and the eyes.

During the progress and the postoperative course of cranial injuries, a systematic ophthalmoscopic examination will give the surgeon information of a favorable condition or will put him on guard against complications. Hemorrhagic symptoms may disappear or appear later. An oculomotor paralysis may disappear (a transitory compression of the nerve fibers by blood or exudate which have been absorbed) or it may persist (a bony compression, which remains, or section of the fibers, which have not regenerated); new forms of paralysis may appear, the cause of which, mechanical or infectious, will have to be sought.

Repeated examination of the visual field gives valuable data on the location of the lesions, the importance and the progress of the lesions, as well as the sequelae of the surgical intervention. I am reminded of a case of a Moor who was very much surprised not to be able to read Arabic, a language which he knew very well, and to be able to read Spanish which he knew but slightly. What happened was that his wound destroyed totally the right occipital lobe, with a consequent left homonymous hemianopia. It also caused a partial destruction of his left occipital lobe, with the consequence of a partial right hemianopia. Reading Arabic from right to left was impossible because the visual field was lost on that side; whereas, reading Spanish from left to right (in the direction in which he still had a useful visual sector of the field) was possible.

With reference to the phenomena of cranial compression, repeated ophthalmoscopic examination and measurement of the retinal arterial tension gives pertinent information. Diminishing tension indicates that a subdural hemorrhage is reabsorbed; unchanged tension shows a collapse of the lamina interna; increased tension, a serous arachnoiditis. It is no less interesting to determine the presence of cranial hypotension, following a large loss of intracranial fluid. Many poorly explained cerebral disorders (headache, migrane, and so forth) may be due to this cause and may be diagnosed by the fall in pressure of the retinal arteries.

Joseph J. Pascal,
Translator.

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THE 1947 ACADEMY MEETING

The 52nd annual session of the American Academy of Ophthalmology and Otolaryngology was held at the Palmer House in Chicago, October 12 to 17, 1947. A few more than 3,400 members and guests, some of whom were from the distant corners of the world, registered for the meeting. The weather was kind, although perhaps a little too warm, and the aura of the meeting was cheerful. For a short time at least, the members could forget the distress of the world and the various political and economic conflicts that have been rubbing us into a state of irritability. The excellence of the program, the splendid and numerous instruction courses, the enjoyable social evenings, and a scientific exhibit that was better than average contributed to the evident success of the meeting. Under the able and wise guidance of the president, Alan C. Woods, of Baltimore, and the other officers of the Academy, the scientific sessions were conducted with expedition and dignity, worthy of the important

subjects that were discussed. Dr. Frederick H. Verhoeff of Boston was the guest of honor. His prestige as investigator, surgeon, clinician, and teacher, and geniality and wit assured the members that the choice was a happy one. The affection and respect that the members hold for Dr. Verhoeff was attested to on many occasions during the meeting by prolonged applause and the award of a plaque by the Academy as a testimony to his outstanding service to ophthalmology.

In his president's address, Dr. Woods spoke on the present policies of the specialty board and the national societies in relation to the progress of ophthalmology. He pointed out the great influence of the various boards in the elevation of the standards of training and practice of the specialties during the past 30 years. He deprecated, however, the tyrannical requirement of a certificate by various hospitals, universities, and government services, in order to permit hospital practice, teaching advancement, or extra financial allowances. He suggested that it is now time to reconsider these requirements and to liberalize them. Dr. Verhoeff discussed, in inimitable fashion, the subject of "Some Problems Concerning Convergence." His address showed evidence of deep and prolonged thought on the subject and will deserve careful reading. The symposium on "Psychosomatic Manifestations" turned out to be an agreeable surprise, and those who were repelled by the formidable title, but stayed to listen anyway, were rewarded by the stimulating talks of Dr. T. A. C. Rennie on the "General Aspects," Dr. C. Stewart Nash on "Otolaryngology," and Dr. D. O. Harrington on "Ophthalmology." The members who were not present missed something noteworthy.

The symposium on "Corneal Transplantation" was arranged, logically discussed, and summarized so ably by the collaborators, that it comprises an important and most significant scientific contribution to this widely publicized and spectacular subject. The finding that only 36 percent of 416 cases had a clear transplant will be most sobering to us after all that we have read in the newsprint about keratoplasty. The symposium showed that coöperative clinical studies such as this are of great value and the method should be applied to other subjects as well.

Dr. Otto Barkan's paper on "Technique of Goniotomy for Congenital Glaucoma" was outstanding. His contribution, the value of which is now rapidly being recognized everywhere, has stood the test of time and experience. Goniotomy is here to stay, beyond question, and is the only operation for this distressing and blinding condition that offers much hope for the affected infants. Other papers of ophthalmic interest are likewise worthy of remark, for the quality of the program was unusually good. The moving pictures, however, were disappointing, on the whole, in subject matter and presentation, although the photographic technique was excellent in most cases.

One hundred and nine individual and 30 continuous instruction courses in ophthalmology were given by 163 instructors. A total of 368 hours of instruction was provided, and each course was filled practically to overflowing. The demand for and the attendance of the courses show how valuable the members think they are. Thus, they maintain first place in the affection of the members and guests, who are hungry for such instruction and beg for more each year.

Dr. Francis Heed Adler gave the fourth Jackson Memorial Lecture on the subject of "Paralysis of Vertical Muscles," and Dr. Robert Thompson Tidrick delivered the second Wherry Memorial Lecture on "Advances in Surgical Hemostasis: Evaluation of Absorbable Agents."

Both of the lectures were most ably executed, and the audience was highly rewarded. This feature of the Academy meeting is assuming a conspicuous position in the affairs of the institution.

Two hundred and 64 candidates were admitted to membership this year, of whom 120 were ophthalmologists. Dr. Conrad Berens was chosen as president elect to serve in 1949, Dr. Ralph Rychener was elected first vice president, and Dr. Ray K. Daily was elected third vice president from the ophthalmologists. Cols. Dart and J. E. Ash of the U. S. Army Medical Department, Dr. Charles Sheard of the Mayo Clinic, and Mrs. Helenor Campbell Wilder of the Army Medical Museum, were elected honorary members. The Leslie Dana Medal of the St. Louis Society for the Prevention of Blindness was awarded to Dr. Verhoeff for his great services in the prevention of blindness.

The exhibits of Dr. K. W. Ascher (Aqueous Veins), Dr. Posner and Dr. Schlossman (Glaucoma), and Dr. A. D. Ruedemann (Radium in Ophthalmology) won first prizes in their respective classes. The exhibit by Dr. R. G. Ingalls on "Intraorbital Tumors" received honorable mention. Dr. Benjamin Rones' exhibit on "Ophthalmology in Cartoon" provided a delightfully light and humorous touch. It was cleverly arranged at the entrance to the exhibits and put one in a good humor both on entering and leaving.

The commercial exhibits were numerous and well displayed. Newer pieces of equipment, apparatus, instruments, and devices were to be seen and handled without trouble and in comfort. Their respective merits were the subject of vehement discussions by groups here and there.

The continuous success of these meeting testifies to the efficiency and hard work of the executive secretary, Dr. William L. Benedict, and the staff of secretaries and officers of the Academy. There is no question of the sincere gratitude and appreciation of every member for their great services.

DERRICK VAIL.

THE FINAL OPHTHALMOLOGICAL STUDY COUNCIL COURSE

This summer the third and last Basic Course in Ophthalmology of the Ophthalmological Study Council has been in full cry, housed at Westbrook Junior College, in Portland, Maine. "Cry" is perhaps an inappropriate word, as the students who brought their families, with 30 children in all, had only four of the crying age or young enough to be properly termed "wetting agents." Families with infants occupied a small dormitory by themselves which had a kitchen, icebox, and laundry. Milk and diaper service were in attendance when they arrived. Single men, married couples, and families with children were housed in separate buildings.

The enrollment was the largest of the series, numbering well over 100. In addition, a small number of students came for part of the curriculum. Over half of the United States was represented. The first registrant was the long-distance champion. He had been serving as a medical missionary to Nigeria, in Africa. He drove from California, with wife and children, in a trailer complete with grandmother. In view of the already strained accommodations at the College, the requirement that students reside on the campus was cheerfully waived and this consignment went off to a trailer camp. Another outsider came from Honolulu. There were also seven Canadians. Seventy were veterans of World War II.

From a physical standpoint, it looks as though the course had finally hit upon the

ideal arrangement. Because the college was designed as an educational institution, the facilities were well adapted to the purpose, instead of the rather makeshift accommodations of the previous courses. The housing and food were more generous than the other ventures, yet the college gave the lowest rates so far. Besides the bedrooms, families had a sitting room, and the recreation rooms of the dormitories were also available. The College authorities and the chamber of commerce interested themselves in the entertainment of the visitors. This was not difficult, as Portland is a considerable tourist center, with lakes, mountains, and beaches nearby.

The course opened on the first day without rain for some weeks. Credit for this achievement was claimed by the city manager in a speech of welcome at an outdoor picnic on the opening day, given by the College to all members of the course. Steak was served—more steak, in fact, than was known to exist in this area. Other picnics were arranged, including a New England clambake for one weekend. This is a form of dissipation indigenous to this region, characterized mainly by unlimited quantities of lobsters, clams, potatoes, and corn, cooked in a cairn of hot stones and seaweed on the beach. Dismembering the shellfish is a trick second only to eating with chopsticks, and should be excellent preparation for the more difficult ophthalmic operations.

The faculty was a trifle larger, and, as in the previous courses, the instructors were distinguished teachers from many parts of the country. A few more subjects were added, such as lectures on therapeutics intended to prepare the students better for clinical work as residents and preceptees.

The instructors were surprised by the enthusiasm and industry of the classes. This is, however, only the general experience of all educational institutions engaged in the training of veterans. The pleasant associations of this group, thrown together for an entire summer in this way, should naturally be renewed at future medical meetings, giving the members a ready-made group of friends. It ought to ease some of the curse of the meetings for the women at least. The council are convinced that one factor in keeping up the momentum was the weekly shot in the arm furnished by the interim examinations in the subjects covered.

The Study Council is being pressed to rescind the termination of these courses and hold another here next summer. No decision can be reached until the annual meeting of the Foundation of Vision of which this course is a subsidiary.

S. Judd Beach.

OBITUARY

THOMAS HALL SHASTID, (1866-1947)

Dr. Thomas H. Shastid, ophthalmologist and author, died February 15, 1947, at his home at Duluth, Minnesota, at the age of 80 years. He was born at Pittsfield, Illinois, in 1866. He became his father's medical apprentice at the age of 10 years. From 1883 to 1886, he was a student at Eureka Collge, Eureka, Illinois. He studied medicine at Columbia University and the University of Vermont, receiving his Doctor of Medicine degree with honors at the latter institution in 1888. His B.A. degree was granted him later at Harvard where he graduated cum laude in 1893. He did postgraduate work at the New York Postgraduate Medical School, at the University of Vienna, and the University of Michigan. The degrees of Master of Arts and Bachelor of Laws were granted at Michigan. He received

the honorary degree of Doctor of Science at the University of Wisconsin in 1922.

Dr. Shastid practiced medicine at Pittsfield, Illinois, from 1889 to 1891; at Galesburg, Illinois, from 1894 to 1897; at Fairfield, Illinois, in 1903; Charleston, 1904; Marion, Illinois, 1905 to 1913. He held the chair of professor of History of Medicine at the American College at St. Louis from 1907 to 1912. In 1914, he specialized in ophthalmology and was certificated by the American Board in 1917. He moved to Duluth, in 1922, where he resided until his death.

He was a member of the American Medical Association, American Academy of Medicine, American Medical-Legal and Toxicological Society, American Academy of Ophthalmology and Otolaryngology, American College of Surgeons, American College of Physicians, American Association of the History of Medicine, International Congress of Ophthalmology, Author's League of America, and numerous other societies. Dr. Shastid was an author of note as well as an ophthalmologist, and his score and more of published works cover such subjects as medicine, international peace, and war profiteering. He wrote two autobiographies, as well as several novels. The best known of his novels was *Simon of Cyrene*. He translated numerous medical volumes and journals from German, French, Latin, and Greek, and was a frequent contributor to scientific journals of all kinds. He also contributed heavily to the American Encyclopedia of Ophthalmology.

Dr. Shastid was an enthusiastic bibliophile. His library at the time of his death contained some 15,000 volumes and covered a wide variety of subjects. Every volume was carefully and systematically indexed. Book lovers gathered from far and wide when it was learned that his library was to be sold. There were books on slavery, witchcraft, medicine, law, literature, philosophy, theology, history, music, and numerous other subjects. There were a number of rare old volumes including *Fitz-Herbert's Justice*, published in 1541. The library also included a collection of letters and signatures of famous people. Among them were a number of original copies of Abraham Lincoln's law briefs written in his own handwriting, a personal letter from Jefferson Davis, and communications from Henry Ward Beecher and John Jacob Astor. Dr. Shastid's wife died in 1940. After her death, he devoted much of his time to his books. Surviving him are an adopted daughter, Mrs. Donald R. Husband of Eugene, Oregon; two brothers, John S. Shastid, Kansas City, Kansas, and Joseph Shastid, Pittsfield, Illinois; and a nephew, John B. Shastid, New Castle, Pennsylvania.

A. C. Hilding.

BOOK REVIEWS

SENSORY MECHANISMS OF THE RETINA. With an appendix on electroretinography. By Ragnar Granit, M.D. New York, Oxford University Press, 1947. 412 pages, 178 illustrations, bibliography, and index. Price, $11.00.

For the past 20 years Professor Granit and his many co-workers in the Royal Caroline Institute at Stockholm have zealously investigated the electrophysiology of the retina. The remarkable achievements in this field are now systematically and lucidly expounded. Probably the ophthalmologists of tomorow will be as familiar with the pattern and interpretation of the electroretinogram as the internists of today are with the electrocardiogram. A pioneer text on clinical electroretinography has already appeared (Karpe, 1945), and Granit confidently predicts that the time will come when the record-

ing of the electroretinogram will be one of the standard methods of every well-equipped ophthalmic clinic, particularly in cases where, owing to opacities of the media, there is difficulty in making an ophthalmoscopic examination or using subjective tests.

The only means of securing information about the fast processes occurring in the retina itself lie in the electrical changes. Discrimination of intensity and contour are functions of the frequency and pattern of the optic-nerve discharges, respectively. The phases of excitation and inhibition emphasize the intensity gradient and give the higher centers the clue for sharpening impressions. The electroretinogram provides an objective basis for the analysis of visual sensation, and in the inter-relations of intensity, area, and duration of the stimulus have amplified the conclusions obtained through subjective methods. Various studies, including that of the pure rod retina of the guinea pig, indicate that besides the rods which accurately reflect the course of visual purple regeneration there are others, "cone" rods, which remain active after light adaptation, the difference being, apparently, wholly at the photochemical level.

A product of Granit's research is his challenging "dominator-modulator theory" of color vision. The scotopic curve is the only one obtainable from the dark-adapted eye, but in the light-adapted state certain elements show with his microelectrode technique restricted sensitivity curves, which Granit terms modulators. So far seven types of modulators have been found—two in the red, three in the green, and two in the blue. Units related to the rods appear responsible for the reception of short-wave lengths. Hue discrimination is best at 5,800 to 6,000 A.U., and 4,800 to 5,100 A.U., where the modulator curves overlap. The dominator curve represents the interaction of closely linked modulators acting as a functional unit. Such convergence could be the result of lateral connections through the amacrine cells, or synchronized impulses. The dominator and modulator mechanisms produce the fundamental sensations of brightness and color, respectively, which are to some extent independent of each other, as shown in deuteranopic color-blindness.

The numerous graphs which at first glance give the book an abstruse and formidable appearance are actually simple, carefully selected, and serve well in bringing the laboratory to the reader.

James E. Lebensohn.

EYE SURGERY. By H. B. Stallard, M.B.E., M.D., F.R.C.S. Baltimore, Maryland, The Williams & Wilkins Co. 444 pages, 338 illustrations. Price, $11.00.

This new book on surgery of the eye is well worth the careful scrutiny of the ophthalmic surgeon. Most of the standard procedures are clearly and concisely given. As one would expect, the drugs and routines are more English than American. The emphasis on war surgery is greater than might have been expected in a text for peace time, but this is natural in a postwar surgical presentation. Many illustrative cases are given and these, especially the plastic, are mostly of battle casualties.

The reviewer is not convinced that illustrative cases, unless used very concretely to point out some definite thought, are of great value. No two plastic repairs are exactly the same and perhaps a textbook does well to restrict the number of such cases. This book, however, does not go to great lengths in this matter and most of the material is well chosen.

Some interesting new material is in-

cluded, such as the very simple operation for pterygium used by Sabri Kamel in Egypt in a great number of cases with complete success even in recurrences; and the operation by the late Sir Richard Cruise for chronic simple glaucoma. Among drugs not often used in the United States that are recommended are "novritox," a solution of novocaine, quinatoxine, benzoic acid, Ringer's solution, and adrenalin. For wide dilatation 'mydricaine," a compound of atropine, cocaine, and adrenalin, is suggested.

For intraocular operations the patient is advised to enter the hospital two days before operation. Liquid penicillin is instilled the night before operation.

American surgeons may be somewhat surprised that the method of corneal section with scissors for cataract extractions, now so popular in this country, is not mentioned except as an adjunct when too small a section is made with a cataract knife. In discussing corneoscleral sutures, the reader naturally expects a description of the Stallard suture but is surprised at the omission of the McLean. The important surgery of retinal detachment will be found to coincide very closely with that practiced in this country. The use of a long needle in cases of high detachment is advocated "so that its point reaches the retina, or nearly so, but does not pass through it." This sounds somewhat theoretical to the reviewer. The use of pinhole spectacles is advocated postoperatively, but advice as to how long they are to be worn is missing.

A chapter is devoted to traumatic surgery, chiefly military. The posterior route for removal of intraocular foreign bodies in the vitreous is the method of choice according to Stallard, differing from the practice current in the First World War.

All in all this text seems sound and well presented. It is a good supplement to one's surgical library.

Lawrence T. Post.

ALTERATIONS DE LA RÉTINE EN RAPPORT AVEC LES AFFECTIONS GENERALES. By Paul Bonnet. Report presented to the Societe Francaise d'Ophtalmologie, May 18, 1947.

The first volume of this most praiseworthy atlas of ophthalmoscopy was reviewed in the March, 1947, issue of the JOURNAL. This second volume is no less interesting. It follows the same plan as its predecessor and is equally well printed. There are 253 pages of text with 41 illustrations. There are 83 beautiful, interesting, and instructive fundus drawings on 36 plates.

The lesions discussed are predominantly associated with disturbances of the hematopoetic system, namely, anemias, leukemias, angiomatosis, hemolytic icterus, Banti's disease, and a few less closely related syndromes.

F. H. Haessler

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below, which broadly correspond to those formerly used in the Ophthalmic Year Book. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. General methods of diagnosis
2. Therapeutics and operations
3. Physiologic optics, refraction, and color vision
4. Ocular movements
5. Conjunctiva
6. Cornea and sclera
7. Uveal tract, sympathetic disease, and aqueous humor
8. Glaucoma and ocular tension
9. Crystalline lens
10. Retina and vitreous
11. Optic nerve and toxic amblyopias
12. Visual tracts and centers
13. Eyeball and orbit
14. Eyelids and lacrimal apparatus
15. Tumors
16. Injuries
17. Systemic diseases and parasites
18. Hygiene, sociology, education, and history
19. Anatomy, embryology, and comparative ophthalmology

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UVEAL TRACT, SYMPATHETIC DISEASE, AND AQUEOUS HUMOR

O'Donnell, J. M. **Behcet's triple syndrome.** M. J. Australia, 1947, June 14, pp. 730-732.

The author reports a case of Behcet's syndrome. The patient had small punched out ulcers of the scrotum and mouth, conjunctivitis, iritis, epididymitis, geographical tongue and gastric disturbances. High doses of ascorbic acid helped in the recovery.

Irwin E. Gaynon.

Rados, Andrew. **Central pulverulent (discoid) cataract and its hereditary transmission.** Arch. of Ophth., 1947, v. 38, July, pp. 57-77.

The author gives a detailed description of this type of cataract (also known as Coppock or Doyne cataract) and analyzes the hereditary transmission. The family trees reported in this paper and the literature show that the mode of inheritance is dominant. (9 figures, 31 references.) R. W. Danielson.

Rio Cabanas, J. L. **Bilateral metastatic pseudoglioma.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 380-384.

An infant, 26 months of age, developed an acute febrile exanthema, with nephritis. The exact nature of the infection was not diagnosed, but it was probably a streptococcus septicemia. A few days after the onset of the disease both eyes developed symptoms of a violent uveitis with hypopyon, and soon afterwards a yellowish conglomerate mass resembling a glioma appeared in the vitreous of each eye. The diagnosis of a metastatic pseudoglioma was made, and the outcome was atrophy of one eye, and doubtful light perception in the other. It is believed that penicillin therapy prevented the development of a panophthalmitis. Ray K. Daily.

Solanés, M. P. **The Vogt-Koyanagi syndrome.** Anales de la Soc. Mexicana de Oft., 1947, v. 5, Jan.-March, pp. 12-23.

The new cases of this disease now reported raise to nine the number

placed on record in Mexico. The ages of these two patients were respectively 25 and 28 years. The former was five and a half months pregnant.

The symptoms included various forms of uveitis; poliosis of the eyelashes, eyelids, and axillas; alopecia and vitiligo; hyperacusia, dysacusia, and deafness, in addition to general neuropathic and febrile manifestations.

Slow recovery of vision occurs, but the vision never returns to normal. Occasionally there is secondary glaucoma, or phthisis bulbi. (References.)

W. H. Crisp.

Stine, G. H. **Detachment of the choroid and the retina. Anatomic and other considerations in the differential diagnosis.** Amer. Jour. Ophth., 1947, v. 30, July, pp. 897-907. (See Section 10, Retina and vitreous.)

Stocker, F. W. **Experimental studies on the blood-aqueous barrier.** Arch. of Ophth., 1947, v. 37, May, pp. 583-590.

It has been demonstrated by numerous authors, especially by the splendid work of Duke-Elder and Friedenwald and their co-workers, that the penetration of the various constituents of aqueous through the blood-aqueous barrier follows a rather complicated scheme. Electric charge, size of the molecule and possibly other factors influence the ratio of transmission of each constituent. But, on the other hand, it has also been shown that any change of the permeability of the blood-aqueous barrier will affect all constituents to a certain extent, though not equally, whether they are electrolytes, nonelectrolytes or proteins.

There is little doubt that the permeability of the blood-aqueous barrier plays an important part in certain cases of glaucoma. It also is known and confirmed by the experiments in part II of this study that the drugs generally spoken of as miotics not only contract the pupil but also increase the permeability of the blood-aqueous barrier.

From this preliminary report, the following conclusions seem to emerge: (1) no appreciable influence on the permeability of the blood-aqueous barrier can be demonstrated when normal rabbits are fed large doses of rutin for three weeks, and (2) the action of physostigmine, which is known to increase the permeability of this barrier after being instilled into the conjunctival sac, is greatly reduced if the animal has been rutinized. (2 charts, 17 references.)

R. W. Danielson.

Vanzetti, G., and Seidenari, R. **The composition of the aqueous humor, particularly the glucose and chloride content.** Rassegna Ital. d'Ottal., 1947, v. 16, Jan.-Feb., pp. 65-77.

Chemical determinations by means of micromethods were made upon samples of 0.88 cc. of aqueous in a series of normal and pathologic eyes. Details of the procedure and results of individual determinations are given in the article. The average chloride content was found to be the same as that of the blood serum, 6.499 gm. per 1,000 cc. and of glucose 0.727 gm. The latter figure is sensibly lower than that given by Ash and less than the percentage in the blood. No appreciable change in the protein content was found. (2 tables, 19 references.)

E. M. Blake.

Vianna, Louzada. **Tuberculin therapy in the uveitides.** Rev. Brasileira de Oft., 1947, v. 5, June, pp. 195-207.

The author believes the following facts should be kept in mind in dealing with the possibility of a tuberculous

etiology: Tuberculous infection is the rule and its existence in the adult may be assumed. This disease in the eye may frequently take on the appearance of an ordinary inflammation without specific character. Tuberculin has curative action in certain tuberculous processes.

The author has studied 142 cases of endogenous affection of the uveal tract, in the past 18 months. Many had had antisyphilitic treatment and others were still undergoing such treatment. Eighteen cases are summarized as having supported the belief that improvement obtained was clearly associated with tuberculin therapy. The tuberculin is kept in dilutions running from 1 to 10 up to 1 to 1,000,000, which are in practice referred to as 1—zero up to 6—zero. (References.) W. H. Crisp.

Vidal, F., and Brodsky, M. **Physiopathologic considerations concerning a case of post-traumatic anisocoria.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Aug., p. 235.

After a gunshot wound of the neck, a patient presented an arteriovenous aneurysm of the left carotid artery, with exophthalmos, conjunctival hyperemia, marked vascular engorgement of the fundus and slight peripheral contraction of the nasal field of the same side. There was also ptosis of the upper lid and miosis due to a lesion of the cervical sympathetic fibers. Resection of the aneurysm brought about gradual improvement of the exophthalmos and vascular disturbances, but the ptosis and miosis remained unchanged. Pharmacologic tests confirmed the sympathetic nature of the latter condition. (Bibliography.)

Plinio Montalván.

Yasuna, E. R. **Danger of penicillin therapy in active uveitis.** Arch. of Ophth., 1947, v. 37, May, pp. 598-607.

A review of the literature of the use of penicillin in various eye diseases is followed by two case reports of uveitis in which the penicillin seemed to hinder rather than favor the healing process. The author explains this apparent action by mentioning the recent theories that uveitis is caused by bacterial toxins and products of bacterial degeneration rather than by the bacteria.

Thus destruction of the bacteria in the focus of infection could aggravate the uveitis.

He concludes that penicillin in the treatment of uveitis does not appear to offer any advantages over previous methods and may cause the uveitis to persist longer than it would otherwise. (41 references.) R. W. Danielson.

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GLAUCOMA AND OCULAR TENSION

Baillart. **Infantile glaucoma in a national institution for the young blind.** Ann. d'Ocul., 1947, v. 180, May, pp. 257-262.

This analysis of 40 patients with infantile glaucoma shows that the tension was surgically brought to normal in only half of those operated upon. Blindness is not only caused by increased ocular tension but also by subsequent atrophy. Twenty-three percent of the patients admitted between the ages of 8 and 18 years had infantile glaucoma. Boys were affected more frequently than girls in the ratio of five to three.

Only five percent of the total infantile glaucomas were due to congenital syphilis and an equal number occurred in children whose mothers had rubeola in the first months of pregnancy. In 17 percent of the cases the infantile

glaucoma was familial. Latent or actual hydrocephalus was associated in approximately 25 percent and buphthalmos existed with infantile glaucoma in 67 percent. Nine eyes had been enucleated before admission and 60 percent of the patients who had had surgical treatment were totally blind.

Chas. A. Bahn.

Bárány, Ernst. **The influence of local arterial blood pressure on aqueous humor and intraocular pressure. An experimental study of the mechanism maintaining intraocular pressure.** Acta Ophth., 1947, v. 25, pt. 1, pp. 81-94.

This second investigation in this field deals with the recovery of intraocular pressure, arterial blood pressure, and heat dissipation by the external ear after unilateral carotid ligation. The former investigation demonstrated that immediately after ligation the intraocular pressure maintains a constant level about 3.5 mm. below normal. The tabulated data of the results of the present study show that the intraocular pressure does not undergo any significant changes within the first 24 hours after ligation. During the following days a slight additional fall in blood pressure and intraocular pressure is followed by a return to normal. The intraocular pressure becomes normal more rapidly than the blood pressure. In some cases the intraocular pressure returns to normal, and the blood pressure remains considerably reduced. The difference in the progress of recovery of intraocular pressure and blood pressure is interpreted as an indication that the intraocular pressure has a defense mechanism against a fall in blood pressure, which enables the intraocular pressure to become normal in spite of a persistent and marked fall in blood pressure. The heat dissipation from the external ears and the ear pressure behave like intraocular pressure. They recover much more rapidly than the blood pressure, and become normal simultaneously with the intraocular pressure. The similarity in the behavior of two completely different circulatory functions supports the view that the recovery of intraocular tension is due not to a slow acting regulation of the intraocular pressure, but to a general adaptation of the vascular bed to a low blood pressure. (7 graphs.)

Louis Daily, Jr.

Barkan, Otto. **Cyclodialysis, multiple or single, with air injection—an operative technique for chronic glaucoma.** California Med., 1947, v. 67, Aug., pp. 78-83.

Cyclodialysis is indicated in primary glaucoma of the wide angle type, and is the operation of choice in cases of narrow angle glaucoma with peripheral adhesions. It is also indicated in certain types of secondary glaucoma, and in eyes in which other types of glaucoma operations have failed. In primary glaucoma the tension was normalized in 63 of 70 eyes. Of these 13 had the narrow angle type with peripheral adhesions, and all were normalized.

With the use of air injection immediately after the cyclodialysis, hemorrhage is controlled, the cleft is visible, and by restoring and deepening the anterior chamber, multiple cyclodialyses are made possible. Maximal miosis is maintained preoperatively and postoperatively, and a miotic is prescribed permanently to assure maintenance of the cleft and channel.

O. H. Ellis.

Barkan, Otto. **Cyclodialysis, multiple or single, with air injection.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1063-1073. (4 figures, 11 references.)

Barry Rodríquez, Julio. **Complex forms of glaucoma.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, June, pp. 576-585.

The importance of the investigation of glaucoma is stressed in all cases of optic nerve atrophy especially in those of unknown cause. The author reports the case of a 67-year-old man who for several years was thought to have a simple bilateral optic atrophy. The diagnosis of glaucoma was made by means of the measurement of ocular tension and visual fields.

J. Wesley McKinney.

Biozzi, Giuseppe. **Cyclodiathermy-puncture.** Riv. di Oftalm., 1946, v. 1, Nov.-Dec., pp. 679-697.

Biozzi performed Vogt's operation on 31 patients. He used the original technique but extended the operative area over one half of the circumference, and applied 150 to 200 single punctures each time. The safety margin between doses that efficiently reduce pressure and dangerous hemorrhage is small. A current of 60 milliamperes was used. The author used cyclodiathermy puncture in 16 cases of chronic simple glaucoma, 12 of absolute glaucoma, 6 of glaucoma in aphacic eyes, 2 of secondary glaucoma, and one each of malignant, chronic irritative, and prodromal glaucoma. In the eyes with chronic simple glaucoma, the cyclodiathermy reduced the intraocular pressure ten times for a period of three to eight months, in three other eyes the period of postoperative observation was too short for conclusive classification, and in three a reduction of pressure lasted for about one month, when a second operation was followed by a pressure drop that lasted 2 and 10 months respectively. In three of the eyes with absolute glaucoma, the operation was a failure, but the other eyes became painless and softer for at least some months. In two of the aphacic eyes, the pressure was controlled for 7 to 19 months; in one eye a second operation became necessary. The cyclodiathermy puncture may save some glaucomatous eyes that would otherwise be lost, and is indicated particularly after failure of other antiglaucoma operations. K. W. Ascher.

Bloomfield, Sylvan. **Relative deficiency of parasympathomimetic activity in aqueous of eyes with chronic simple glaucoma.** Arch. of Ophth., 1947, v. 37, May, pp. 608-617.

The purpose of this investigation was to determine experimentally whether a parasympathomimetic substance actually occurred in the nonglaucomatous human eye and to determine its identity if present. A series of eyes with chronic simple glaucoma was also studied to explore the possibility that some deficiency in the normal activity of such a cholinergic substance occurred in that disease. Since the aqueous humor is, in a sense, a perfusion fluid of the eye, and, with proper precautions, is safely obtainable by paracentesis from the living organ, the study of that fluid seemed suited to this purpose. Because of the pharmacologic nature of this investigation and the extreme dilution of the substances which are studied, biologic methods of assay were employed.

In 17 of 20 nonglaucomatous eyes with various noninflammatory pathologic conditions, an appreciable parasympathomimetic effect was demonstrable in the aqueous humor.

In each of seven eyes in which the aqueous humor could be further studied, this cholinergic activity was found to be due to the presence of acetylcholine.

In 15 of 20 eyes in various stages of chronic simple glaucoma, no such parasympathomimetic activity could be demonstrated in the aqueous humor. In the remaining five eyes in this series, the intensity of the parasympathomimetric activity present was significantly lower than that which occurred in the aqueous of the 17 nonglaucomatous eyes which produced cholinergic effects.

This relative deficiency of parasympathomimetic activity of the aqueous humor in eyes with chronic simple glaucoma was not altered by the successful treatment of the disease with various filtering operations.

There is evidence that this relative deficiency in parasympathomimetic activity of the aqueous of eyes with chronic simple glaucoma is related to the faulty regulation of intraocular pressure which occurs in that disease. (8 references, 4 figures.)

R. W. Danielson.

Bloomfield, Sylvan, and Kellerman, Leo. **The relative value of several diagnostic tests for chronic simple glaucoma.** Amer. Jour. Ophth., 1947, v. 30, July, pp. 869-877. (8 figures, 17 references.)

De Torres Lucena, M. **Influence of atropine given intravenously on the ocular tension of primary glaucoma.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 446-454.

This study was made on 62 patients with primary glaucoma, between the ages of 60 and 70 years. Intravenous injection of atropine sulphate in doses of 0.25, 0.50, and 0.75 mg. were given every six or seven minutes until the total amount reached was the amount given in the Vasquez-Danielopolu test. The ocular tension and pupillary measurement were taken every 20 minutes in the first two hours and every hour thereafter until six were made. Hypotension was found in 34.1 percent, hypertension in 51.2 percent, and no deviation in 14.6 percent. All but three responded with mydriasis before the first two hours. In order to prevent a later hypertension, drops of 7-percent pilocarpine were given after the fifth hour.

J. Wesley McKinney.

Diaz Domínguez, Diego. **Spontaneous healing of glaucoma.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 455-467.

The author reports in detail three cases of chronic glaucoma which had healed spontaneously.

J. Wesley McKinney.

Dunphy, E. B. **Di-isopropyl fluorophosphate in glaucoma.** Bull. New England Med. Center, 1947, v. 9, June, pp. 102-106.

DFP is a powerful, toxic miotic. The miosis persists up to 14 days and is present under full dark adaptation. It acts by destroying cholinesterase and reduces the tension in glaucomatous and normal eyes. In one-half of the eyes with glaucoma which did not respond to pilocarpine or eserine, DFP succeeded in bringing the tension to normal. Its ontoward effects are pericorneal injection, congestive iritis, and, occasionally, an increased ocular tension.

Irwin E. Gaynon.

Gallenga, R. **The operability of advanced chronic glaucoma.** Rassegna Ital. d'Ottal., July 1943-Dec. 1945, v. 12-14, pp. 516-528.

Gallenga urges surgery in all cases of chronic glaucoma, regardless of the duration of the disease or the state of the fields of vision. He favors the fis-

tulizing type of operation. When the tension is very high a cyclodialysis is added to the trephine operation. He agrees with Lauber that there is a relationship between ocular tension and general arterial pressure, and takes measures to raise the latter when it is below normal. When one cannot lower the tension and raise the blood pressure, operation results in decrease of vision and fields. The author gives a formula for prognosticating the results of surgery based on the ocular tension, the retinal arterial pressure and the general blood pressure.

Eugene M. Blake.

Granville, Roberto. **Goniodialysis.** Rev. Brasileira de Oft., 1947, v. 5, June, pp. 231-235.

The author's operation for chronic glaucoma secondary to anterior synechia consists of making a scleral incision with the lance keratome or the Graefe knife, 2 mm. from the limbus and 4 mm. long; and then passing a spatula through this incision into the anterior chamber and sweeping the spatula along the angle of the chamber, first for a quarter of the limbal circumference to one side and then similarly to the other side of the primary incision. The spatula, maintained in intimate contact with the posterior face of the sclera, should not penetrate beneath the sclera more than 2 mm. from the limbus. Two successful and two unsuccessful cases are reported. (2 illustrations.) W. H. Crisp.

Just Tiscornia, Benito. **Exploration of the functional status of the arterioles, capillaries, and veins of the anterior ocular segment.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 367-374.

This is essentially a review of the work of Vidal and Malbran on vasoscopy. Reference is made to Vidal and Malbran's conception of the role of the various components of the vascular system in the maintenance of ocular tension. The ocular tension of 100 mm. Hg found immediately after death is considered the static ocular tension produced by the fluid content of the interstitial tissues. The pressure above that is designated as dynamic, and attributed to active circulatory processes, in which the capillaries perform the most important function. In angiosclerosis involving the arterioles the ocular tension is low, but if the disturbance involves principally the veins the ocular tension rises.

The tests for the functional integrity of the ocular arterioles, capillaries, and veins are described in detail. For the study of the ocular arterioles, which are stimulated by the fibers of the sympathetic, 5-percent ephedrine sulphate solution is instilled into the conjunctival sac five times, at intervals of one minute. The ocular tension and size of the pupil are noted before the instillation, and 20 to 60 minutes afterwards. In normal persons and in advanced angiosclerosis there is no effect. In a disturbance of the venous circulation there is a rise in the ocular tension. In neuro-circulatory asthenia, with a diminished blood supply, there is a lowered ocular tension. The ocular circulation may be improved by conjunctival instillation of 2-percent ephedrine sulphate combined with calcium chloride. The capillary activity is under control of the parasympathetic system in which acetylcholine is the chemical intermediary. One can substitute carbaminoilcholine for acetylcholine by the instillation of a one third-percent solution preceded by a wetting agent; this instillation affects ocular tension through

capillary action. In patients with a normal circulatory apparatus there is a rise in tension for three to five minutes which is produced by increased arterial capillary activity. Following the short rise is a slow fall in tension lasting 50 minutes; this fall is ascribed to the increased activity of the veins, which carry away intraocular fluid more rapidly than it enters. About 80 minutes from the beginning of the test tension begins to return to normal, which it reaches at the end of three hours. In inadequate venous activity the secondary fall in tension does not take place.

Another test determines the cholesterinase content of the anterior ocular segment. A drop of 1.8-percent solution of dimethylcarbamic ester of bromide of oxipheniltrimethilammonia is instilled in conjunction with a wetting agent. Within eight minutes the tension rises 3 mm. because of increased arterial capillary activity. After two to three minutes the tension returns to normal, as a result of increased activity of the venous capillaries. Normally the effect of the drug is insignificant. In incipient glaucoma the effect manifests itself chiefly on the pupillary sphincter and ciliary muscle. In advanced glaucoma the secondary fall in tension does not occur. Vidal and Malbran believe that the first change in primary glaucoma is an increased cholesterinase content in tissues which contain it normally, such as the retina, the iris, and the ciliary body; later as its quantity increases, it is found in the aqueous and the vitreous which do not contain it normally. The increased cholesterinase content leads to the circulatory disturbances and ocular edema that characterize the glaucomatous syndrome. The tests of vascular function demonstrate metabolic changes in the anterior ocular segment. Ray K. Daily.

Kalt, Marcel. **Iridencleisis in the treatment of secondary glaucoma.** Arch. d'Opht., 1947, v. 7, no. 1, pp. 18-27.

Kalt reviews the surgical procedures which have been used in glaucoma secondary to iridocyclitis and concludes that repeated paracentesis, iridectomy, cyclodialysis, and the corneoscleral trephine are inefficacious. He advocates iridencleisis, performed according to the method of Weekers, as the surgical procedure of choice. In 22 cases of iridocyclitis with secondary glaucoma he was able to control tension in 86 percent. In 60 percent of the cases there was an improvement in vision and in 50 percent of the cases the preoperative visual fields were maintained.

Phillips Thygeson.

Magitot, A. **Thalamus and glaucoma.** Ann. d'Ocul., 1947, v. 180, Jan., pp. 1-9.

After 60 years of research, glaucoma continues to be ophthalmology's enemy number one. Due to the emphasis of corneoscleral filterability by the Heidelberg School, the vascular factor in glaucoma has been neglected. This factor largely determines the response of the individual eye to intraocular tension. As it is the intraocular venous pressure and not the arterial that is about proportionate to the intraocular tension, the vascular process is apparently primarily venous. The genetic degeneration of the intraocular vascular system is only part of a similar condition elsewhere in the body, as has been demonstrated by subungual capillaroscopic tests. Especially the metabolism of water and acetylcholine is involved. The frequent association of glaucoma with endocrine disturbances, especially those of the pituitary gland, is thus explained. Eyes structurally predisposed to glaucoma are hypersen-

sitive to sympathetic and parasympathetic stimuli in which the ductless glands play an important part. Bodily vascular hypersensitivity is closely associated with that of some of the diencephalic centers especially those in the thalamus. Here sensory perceptional and other stimuli are integrated into autonomic vascular responses with their attendant production of sympathetin, acetylcholine and related substances. This thalamic hypersensitivity which is partly vascular helps us to better understand why pain and emotion, febrile intoxications such as epidemic dropsy, and the use of caffeine may precipitate or aggravate glaucoma.

The treatment of glaucoma is based chiefly upon the use of drugs which alter autonomic vascular function. Decompressing operations alone do not eliminate this vascular factor and therefore do not cure glaucoma. The psychoneurologic treatment as an adjunct to other means is becoming increasingly important. It is important in this treatment to make the patient realize that if he remains calm he increases the chance to avoid his potential blindness.

Chas. A. Bahn.

Malbrán, J. L., and Caretti, J. A. **Glaucoma: early diagnosis. The vacuum cup test.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Oct.-Nov., p. 315.

The authors studied the value of the vacuum cup test of Werner Herzau as applied by Abreu Fialho to the early diagnosis of glaucoma. The vacuum cup is made of plastic material and is connected to a rubber bulb for the production of a vacuum. It is placed over the cornea of the eye under study and the vacuum is maintained for a period of five minutes, after which the behavior of the intraocular tension is studied with the tonometer. In normal eyes there is a drop in tension immediately after the test to half or less of the original. The period of recovery lasts from 5 to 15 minutes during which the tension returns to the initial level, but never above it. In eyes with a very delicate conjunctiva, bulbar hemorrhages and edema may occur after the test and disappear in three to five days. After studying this test in normal and preglaucomatous eyes the authors conclude that any eye whose tension does not behave in the characteristic manner, must be considered as suspicious of preglaucoma. Eyes must be also considered as suspicious of preglaucoma when the tension falls, but recovers in five minutes or less, or if after the recovery, the tension climbs 10 mm. or more higher than the original figure.

The vacuum cup test is a valuable adjunct in the diagnosis of preglaucoma, but is not conclusive as a sole procedure. Its mechanism is unknown and Abreu Fialho advanced the theory that the neurovegetative nervous system is an important factor in it. No untoward effects have been observed after the test. (1 illustration, charts, bibliography.) Plinio Montalván.

Marlow, S. B. **Field of vision in chronic glaucoma.** Arch. of Ophth., 1947, v. 38, July, pp. 43-56.

In 1931, observations on 11 cases of chronic glaucoma showing the effect of reduced illumination on the field of vision were reported by the author. The present review has to do with 50 additional cases studied by the same method. Marlow concludes that the necessity for control of the illumination in examination of fields of vision in cases of chronic glaucoma would seem obvious; yet too little attention has been directed to it. The amount of light available should be recorded, whether

natural daylight or artificial illumination is used. The value of reduced light in demonstrating early field defects characteristic of glaucoma in what Traquair calls the preperimetric stage of the disease is suggested by the charts and the analysis of the cases studied. Ferree and Rand have used 7 foot candles in their perimeter and tangent screen, but in this study 0.02 foot candle was selected. (13 charts.)

R. W. Danielson.

Morano, M. **Glaucomatous changes of the lens.** Boll. d'Ocul., 1946, v. 25, July-Sept., pp. 359-380. (See Section 9, Crystalline lens.)

Morano, M. **The physiologic action of prostigmin.** Rassegna Ital. d'Ottal., July 1943-Dec. 1945, v. 12-14, pp. 468-503.

The author experimented with prostigmine intravenously and orally in normal and glaucomatous eyes. Administered parenterally, prostigmine causes miosis in normal eyes and in those in which adrenalin had been instilled, but has no effect upon atropinized eyes. The drug is effective especially in glaucoma complicated by vascular changes in the fundus, even in the post-thrombotic type.

The intravenous use of prostigmine lowers the general blood pressure, and, therefore that of the retinal circulation, and has proved beneficial in embolism of the central retinal artery. According to Morano a 1-percent solution of prostigmine is as equally effective as a 1-percent solution of eserine or 3-percent pilocarpine. Eugene M. Blake.

Moreu, Angel. **Experience with goniotrabeculotomy and goniocyclodiathermy.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 468-478.

The author thought that better results could be obtained in glaucoma by combining the cyclopuncture diathermy of Vogt and the goniotrabeculotomy of Barkan. Instead of using the Ziegler's knife he used a diathermic needle which is easier to manage. The scar left by this procedure is softer and more flexible, the hemorrhage is eliminated and the occurrence of infection is minimal. The operation can be repeated if it becomes necessary. A series of four cases is reported. From this study the author concludes that the proper selection of suitable cases is important. Eyes with absolute glaucoma and a narrow angle or with peripheral total synechia do not respond well. Glaucoma with wide angle and edematous zones of the ciliary body responds favorably. Intraocular hypertension follows the operation. This may last for 24 hours and is followed by lowering of the tension. It is not recommended to do more than six punctures, because sometimes it is necessary to operate again. The pupil must be in miosis and the use of miotics must be continued for the first 48 hours after the operation. Postoperative medical therapy is always necessary.

J. Wesley McKinney.

Moreu, Angel. **The mechanism of action of antiglaucomatous operations.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 479-486.

The author states that there are antiglaucomatous operations which are very useful even though no fistulization is produced and the drainage is not increased. Such operations are iridectomy, cyclodialysis, diathermic punctures, goniocyclodiathermy and goniotrabeculotomy. It has been proved many times by means of gonioscopy that iridectomy does not free the iridocorneal angle. The same results have

been obtained by performing sphincterectomy which conserves the iris root. The cyclodialysis does not make either a tunnel or a fistula. A short time after the operation is performed the tunnel is obliterated by a small blood clot and the ciliary body is firmly joined to the sclera which sometimes gives an evident peripheral synechia. Everybody agrees that diathermic punctures and goniocyclodiathermy do not produce any drainage. Barkan says that goniotrabeculotomy would serve for opening the sclerosed wall of Schlemm's canal but the author repeats that in this type of operation the opening will close after a short period just as in cyclodialysis. Sometimes fistulization operations have been performed in which no filtration bleb has been observed. However, the tension of the glaucoma has been controlled. Undoubtedly these operations act upon glaucoma by a more complex mechanism than the mere establishment of drainage. The author agrees that all antiglaucomatous operations have a common mode of action; they act directly on the ciliary body by modifying its innervation or vascularization, and indirectly on the eyeball. He concludes that postoperative medical therapy is always necessary for the success of surgical treatment.

J. Wesley McKinney.

Shaffer, R. N. **Inverse cyclodialysis.** Amer. Jour. Ophth., 1947, v. 30, July, pp. 860-868. (11 figures, 1 table, 11 references.)

Sugar, H. Saul. **Cyclodialysis: a follow-up study.** Amer. Jour. Ophth., 1947, v. 30, July, pp. 843-859. (2 tables, 3 charts, 55 references.)

Thomassen, Thore Lie. **Experimental investigations into the conditions of tension in normal eyes and in simple glaucoma, particularly performed by subjecting the eyes to weight compressions.** Acta. Ophth., 1946, Supplement 27.

This monograph is a review of the literature on the effect of compression or massage on the normal and glaucomatous eye, and a report of an exhaustive experimental investigation. In this study compression was produced by Baillart's ophthalmo-dynamometer, placed on the limbus temporal to the cornea, and the tension measured by the Schiøtz tonometer, before compression, and 5, 15, and 35 minutes after compression. A compression of 25 gm. for 2 minutes, and of 150 gm. for 2 to 6 minutes was used in most experiments. During the compression there is a fall in tension, attributed to the forcing out of aqueous from the eye, through the canal of Schlemm. After the removal of compression the tension gradually returns to its initial level, and in some cases it continues to rise, producing a so-called relative hypertension. The latter is believed to be a reaction to the irritation of the compression, acting through the innervation of the ocular vessels, in the form of an increased blood volume, or an increased capillary tone with augmented secretion of aqueous. The result is an increased fluid content of the eyeball. The occurence of relative hypertension in some eyes, and not in others, is explained by the varying faculty of eyes to compensate the effect of the compression. The extent of this power of compensation may be determined by finding the weight of compression required to produce a relative hypertension. The greater compression an eye can bear without producing a relative hypertension, the greater should be its power of compensation. The data show that

the power of compensation diminishes considerably with age, and is completely lost in glaucoma before the tension rises.

In this study all normal eyes withstood a compression of 150 gm. for 2 minutes without developing a relative hypertension, and this degree of compression is therefore taken as the minimum power of compensation for normal eyes. The extent of the fall in tension following compression varies, but is not affected by age. Homatropine reduces the fall during a compression, and pilocarpine increases it. Homatropine also reduces the compensating power of the eye, while pilocarpine augments it. In glaucomatous eyes the power of compensation is greatly reduced, and a relative hypertension may be produced by a compression of 25 gm. for 2 minutes; the result however, is greatly influenced by the phase of ocular tension during which the compression is performed. With compression performed in an increasing phase of ocular tension the fall in tension is small, and the relative hypertension high; in a decreasing phase of ocular tension the compression produces a marked fall in tension and no relative hypertension. This phenomenon was not discovered during former investigations, and accounts, the author believes, for the disparity of reported data. It is explained by the difference in the tension of the intrascleral veins. In an increasing phase of ocular tension, the tension in the intrascleral veins is high and the escape of fluid through Schlemm's canal is blocked. In a decreasing phase the tension in the intrascleral veins is low and the escape through Schlemm's canal becomes easy.

An attempt is made to apply the data obtained in this study to the clarification of some of the glaucoma problems. The author finds that the data indicate that pathogenetically there are two forms of increased ocular tension. In one the tension rises as a result of a change in the ratio between the volume and the contents of the eyeball, such as is produced by pressing the eyelids together; in this form there is no increase in the tension of the ocular capillaries, and the rise in tension is compensated by the escape of aqueous through Schlemm's canal. The second form of increased intraocular pressure is due to a primary increase in the capillary tension, and can not be compensated by aqueous escape through Schlemm's canal. The increased ocular tension in glaucoma, as well as that produced by the provocative tests is of this type. Application of the data to the explanation of the regular oscillation in ocular tension suggests that the changes are due to corresponding changes in the tension of the ocular capillaries, stemming from rhythmical oscillations in a nervous impulse that originates in the central nervous system.

Clinically the use of compression as a provocative test is reliable only when it indicates an increased ocular tension. No fall in tension after compression is indicative of glaucoma. The occurrence of relative hypertension following compression of 25 gm. for 2 minutes is strongly suggestive of glaucoma. A relative hypertension following compression of 150 gm. for 2 minutes suggests the possibility of glaucoma. A negative test is of no value and carries no assurance of normal tension, because the test will also be negative in glaucoma in a decreasing phase of ocular tension. Compression may also be used as an aid in the evaluation of therapy. An eye with a poor power of

compensation should be kept under the influence of miotics even if the tension appears normal. Effective treatment with miotics should produce some power of compensation, and the compression test can be used to determine the required frequency of instillation of miotics. Compression with 25 gm. for 2 minutes is adequate for this test; if there is no relative hypertension after this compression, the therapeutic effect on the ocular tension can be regarded as satisfactory. Ray K. Daily.

Torres Lucena. **Clinical contribution to the knowledge of the etiopathogenesis of primary glaucoma.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, March, pp. 265-287.

A study of 72 cases of primary glaucoma convinced the author that liver disturbances do not play any role in the pathogenesis of primary glaucoma. (90 references.)

J. Wesley McKinney.

Vila Ortiz, J. M. **Intraocular tension and its influence in the appearance of retinal hemorrhages in diabetic patients.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, March, pp. 288-298.

Fifty-one of 99 diabetic patients did not show retinal hemorrhage. Hypotension was found in 22.5 percent of the patients without retinal hemorrhage and 38.5 percent of those who had retinal hemorrhages. The author concludes that diabetic patients generally have a relatively low ocular tension and the incidence of low tension is higher in patients with retinal hemorrhages.

J. Wesley McKinney.

Vidal, F., Malbrán, J. L., and Garcia Badaracco, J. **Experimental acute intraocular hypertension.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Aug., p. 227.

In normal cats under sodium pentobarbital anesthesia given intraperitoneally, the instillation of a 0.33-percent solution of carbaminoylcholine chloride in the eye produces, after a brief initial fall, a very marked increase in the intraocular pressure. (Charts, bibliography.) Plinio Montalvan.

9

CRYSTALLINE LENS

Cantonnet, F. **Critical study of the incision in cataract extraction.** Ann. d'Ocul., 1946, v. 179, Dec., pp. 607-622.

The relative merits of cataract incisions made with the Graefe knife and keratome enlarged with scissors are analyzed in a series of 180 operations. The former was used in 106 cases, and the latter in 74. The complications which occurred at the time of incision are statistically analysed. The chief advantage of the keratome incision is that it can always be placed precisely in the limbus. Delayed healing occurred in 10 percent of the eyes opened with a Graefe knife and in four percent of those incised with a keratome. After six weeks the average amount of postoperative astigmatism as measured with a keratome was: Graefe, 3 diopters, keratome, 2 diopters.

Chas. A. Bahn.

Cristini, G. **The fluorescence of normal and cataractous lenses.** Ophthalmologica, 1947, v. 113, March, pp. 156-164.

Helmholtz was the first (1855) to observe and describe the phenomenon of fluorescence of the crystalline lens. The studies of F. P. Fischer (1934-1935) suggested a relationship between cataract formation and photolytic destruction of the so-called flavines of the lens substances related to vitamin B_2.

The fluorescence phenomenon seemed to be dependent upon the presence of those flavines. For that reason Cristini reinvestigated the fluorescence phenomenon. Cataractous human lenses obtained by intracapsular extraction or clear human lenses from eyes enucleated because of tumors of the sclera, were placed in the path of ultraviolet light obtained from an arc lamp; the rays transmitted and emitted by these lenses were analyzed qualitatively and quantitatively by means of a photometer. The behavior of clear and cataractous lenses was qualitatively the same: the lenses emitted a band of visible rays extending from 501 to 514 millimicrons. Brightness and saturation of this spectral band varied somewhat depending upon the type and stage of the cataract. Lens extracts prepared with water, methyl alcohol or chloroform, showed the same fluorescence phenomenon as whole lenses. These results indicated that the fluorescence of the lens was not dependent upon the physical arrangement of the particles within the lens but upon one or several chemical compounds, present both in clear and cataractous lenses. Exposure of the alkalinized extracts to large doses of ultraviolet light caused only a slight change of the fluorescence which proves that the substance causing the fluorescence is not a flavine, but probably a halloxazine substance. The question now arises: What is the relation of the latter substance to the respiratory enzyme system or to any of the metabolically important constituents of the lens? Peter C. Kronfeld.

Johnstone, I. L. **Familial cataract with extensive pedigree chart.** Brit. Jour. Ophth., 1947, v. 31, July, pp. 385-395.

Five generations of two branches of a family were studied with respect to a strongly persistent familial cataract. In all other respects the people studied were quite healthy and free from other developmental defects. Blood chemistry studies also showed no irregularities. One family branch consisted of 73 persons, 36 male and 37 female. The other branch included 58 persons, 28 male and 28 female (the sex of two members was unknown). Of these 58, 6 males and 11 females were affected. About 31 percent of the members were affected. Sex differences were insignificant. The disease was passed on by affected persons only and is therefore a Mendelian dominant characteristic.

The cataract itself was so characteristic that a person possessing it could be positively identified as a member of the family by examination of the eyes. It was a presenile, posterior, sub-capsular, saucer-shaped opacity which had leaf or feather-like radiations extending from its center, had flakes or dots of various colors, and caused an accentuation of the shagreen of the anterior capsule. It was always bilateral.

Morris Kaplan.

Knapp, Arnold. **Present state of the intracapsular cataract operation.** Arch. of Ophth., 1947, v. 38, July, pp. 1-38.

This excellent paper combines a complete review of the literature and the author's opinions derived from his wide surgical experience. Anatomy, histology, techniques, accessory steps, instruments, complications, advantages and disadvantages are discussed in detail. (77 references.) R. W. Danielson.

Lee, O. S., Jr. **Corneoscleral suture in operations for cataract.** Arch. of Ophth., 1947, v. 37, May, pp. 591-597.

The use of sutures for closure of incisions in cataract operations is one of the most useful and valuable refinements in ophthalmic surgery.

Ophthalmic surgeons do not all agree, however, that sutures aid in reducing the incidence of postoperative hemorrhage into the anterior chamber. Older writers were of the opinion that the bleeding came from the iris. More recent investigations, however, point to the incision as the source of hemorrhage. Any separation of the lips of the wound tears these vessels, and results in bleeding under the conjunctiva or, more frequently, into the anterior chamber.

For the past fifteen years it has been a routine procedure to employ three or more interrupted limbic-episcleral sutures for the closure of incisions in operations for cataract. In 1945 Lee and his associates began to use a modified Liegard suture placed in the 12 o'clock position on the limbus before the incision with the keratome was made, with two additional limbic-episcleral sutures placed on each side of it after extraction of the cataract. The use of this suture has reduced the incidence of hemorrhage into the anterior chamber in cataract extractions from 15.3 percent, when interrupted limbic-episcleral sutures alone were used, to only 6.6 percent, when the Liegard suture was added. When hemorrhages did occur, they were usually less extensive. (12 references, 1 illustration.) R. W. Danielson.

Morano, M. **Glaucomatous changes of the lens.** Boll. d'Ocul., 1946, v. 25, July-Sept., pp. 359-380.

Lens changes are described in 14 eyes examined biomicroscopically in patients affected by glaucoma in its different forms before and after antiglaucomatous surgical procedures had been performed. Aside from exfoliation of the anterior capsule and the acute subepithelial disseminated cataract of Vogt, a third kind of lens change was differentiated. This is the "glaucomatous cataract", which manifests itself as a posterior complicated cataract in primary glaucoma. One of the most important characteristics of the last type of cataract is the deterioration of vision after a surgical procedure. The writer advises examination of the lens with the slitlamp and dilatation of the pupil with adrenaline before attempting a decompressive operation so that the patient may be informed in cases of posterior complicated cataract that deterioration of vision may follow the operation. (Bibliography.)

Melchiore Lombardo.

Moretti, Ezio. **Subluxation of the lens into the anterior chamber in the treatment of total congenital cataract.** Boll. d'Ocul., 1946, v. 25, July-Sept., pp. 402-406.

In the course of the discission of a congenital hard cataract in an infant the capsule was not penetrated by the knife-needle but manipulation of the instrument provoked a partial luxation of the lens into the anterior chamber. The lens was absorbed some time later. It is assumed that in attempting to penetrate the capsule of the lens the zonula was broken and a tear in the posterior capsule was made through which the lens matter was absorbed by the aqueous. Because of the good result the procedure was purposely repeated in the other eye.

Melchiore Lombardo.

Owens, W. C., and Hughes, W. F., Jr. **Intraocular hemorrhage in cataract**

extraction. Arch. of Ophth., 1947, v. 37, May, pp. 561-571.

The authors have reviewed 2,086 extractions of uncomplicated senile cataract performed at the Wilmer Ophthalmological Institute.

In order to determine what factors in the patient's general physical status might predispose to the occurrence of postoperative hemorrhage into the anterior chamber, the cases were analyzed from the following standpoints: (1) age, (2) blood pressure, (3) blood-clotting mechanisms, (4) diabetes, (5) syphilis and (6) foci of infection.

The authors concluded that except for severe diabetes, the general systemic condition of the patient is unrelated to postoperative hemorrhage into the anterior chamber. Operative technics promoting firm closure and avascular healing of the incision reduced the incidence of this complication. These technics include the use of two corneoscleral sutures and a shallow section. The visual results were significantly poorer in the eyes with postoperative hemorrhage into the anterior chamber than in those without hemorrhage. This was chiefly due to persistent opacities in the vitreous. (15 tables, 6 references.)

R. W. Danielson.

Pérez Llorca, J. **Simplification of suction extraction of senile cataract.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 384-389.

Pérez Llorca ascribes the lack of popularity of suction extraction to the need of complicated and expensive apparatus. He designed a simple device, consisting of a canula, with a suction cup at one end, and a rubber tip, similar to that used on a medicine dropper at the other. His experience indicates that the suction produced by the rubber tip is quite adequate to tumble and extract the lens. (3 illustrations.)

Ray K. Daily.

Rivas Cherif, Manuel de. **The voluntary complications of the cataract operation.** Anales de la Soc. Mexicana de Oft., 1947, v. 21, April-June, pp. 60-88.

This paper was previously published in Archivos Medicos Mexicanos (1946, February) and is referred to in some detail in an editorial in the American Journal of Ophthalmology (1946, v. 29, p. 1594) and also under "Correspondence" on page 501 of the April, 1947, issue of the Journal. (Bibliography.)

W. H. Crisp.

Sánchez Mosquera, M. **The use of penicillin as a preventive measure in cataract operation.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, Jan., pp. 48-51.

The author recommends the use of penicillin before cataract operation, especially when some infection is suspected. Penicillin is given intramuscularly, starting 12 hours before the operation and continuing six hours after. The dose is 20,000 units every three hours. He reports seven cases in which good results were obtained.

J. Wesley McKinney.

Ventola, V., and Iribarren, F. **Retinal detachment. Pregnancy and ectopia lentis.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Aug., p. 232.

A patient with congenital ectopia lentis presented in the sixth month of pregnancy a retinal detachment in the right eye. No tear could be found and the fundus of the left eye was normal. In view of the ectopia lentis and the possible etiologic relationship between the detachment and the pregnancy, no

surgery was performed. The final outcome is not reported.

Plinio Montalván.

10

RETINA AND VITREOUS

Aguilar Muñoz, José. **Recurrent edema of the macula (retinitis centralis serosa).** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, June, pp. 586-588.

A man 50 years of age had edema of the right macula three times within three years. On general examination only arterial hypertension was found and it was thought that the edema was due to the metabolic changes brought about by the arterial hypertension. In spite of the recurrence the outcome was favorable. J. Wesley McKinney.

Alvarz Luna, Rogelio. **Berlin's edema and hole of the macula.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, March, pp. 221-225.

The literature concerning the pathogenesis of Berlin's edema is briefly reviewed. A case of a young boy is reported, who suffered a traumatic injury to one of his eyes. The anterior chamber was completely filled with blood and when this disappeared the ocular fundus showed a small pigmented dot in the fovea, which diminished the vision to perception of hand movements at 20 cm. Later he developed a hole in the macula. J. Wesley McKinney.

Appelmans, M. **Pseudo-albuminuric stellate retinopathy in a patient with paraganglioma.** Arch. d'Opht., 1946, v. 6, no. 4, pp. 448-455.

The author describes the case of a man, aged 30 years, who for six weeks had suffered from a great loss in vision. Ophthalmoscopic examination revealed a macular figure with hemorrhages and edema of the nerve head and surrounding tissues. The arteries were contracted and the veins dilated. General examination revealed a hypertension and a slight albuminuria. Kidney function was normal but an abdominal tumor in the left upper quadrant was noted. Surgical removal yielded a heavily vascularized tumor situated under the renal hilus. Histopatholgic examination revealed a non-encapsulated paraganglioma. Within a few days after removal of the tumor the hypertension had diminished, the vision was markedly improved, and the papilledema had disappeared. The macular star, however, persisted for several months. Vision returned to normal in each eye. Subsequently the tumor recurred and, in spite of radiotherapy, progressed. Six years after the surgical intervention the tumor had infiltrated widely although without metastasis. The retina showed no new involvement and visual acuity remained normal.

The author concludes that the pseudo-albuminuric retinopathy was the direct result of this endocrine tumor derived from embryonic sympathetic-system cells. The paroxysmal hypertension with intense headache and pulsation in the eyes was considered to be characteristic of hyperadrenalinism. The resultant angiospasm was assumed to be the cause of the retinal lesion because removal of the tumor caused disappearance of both the hypertension and the retinopathy. Phillips Thygeson.

Arcuri, D. **Retinal detachment in pregnancy.** Rassegna Ital. d'Ottal., July 1943-Dec. 1945, v. 12-14, pp. 275-300.

Three cases of retinal separation that occurred in the sixth, seventh and the eighth month of pregnancy are reported. Two were bilateral, and spon-

taneous reattachment took place in all three. The detachments persisted for from 12 to 20 days.

After thoroughly reviewing the literature the author points out the differences between the clinical picture, the pathogenesis, the course, prognosis and therapy in the separations in pregnancy and in the other forms. Although retinal reattachment occurs without treatment, the prognosis as to vision is not always good. Renal insufficiency of the mother is the most important cause. The detachment may be associated with acute or chronic nephritis and neuroretinitis. (5 colored pictures.)

Eugene M. Blake.

Barrenechea, S., and Contardo, R. **Roentgen therapy of retinal venous thrombosis.** Arch. Chilenos de Oft., 1946, v. 2, July-Oct., pp. 235-241.

The cases reviewed by the author include eleven of thrombosis of a branch, and ten of thrombosis of the central vein of the retina. The etiology was usually arteriosclerosis and the age of the patients varied between 42 and 74 years. Fractional doses of X ray were used, reaching a total of 550 r in thrombosis of the central vein. The initial dose was 100 r. The cases are tabulated in detail, to support the authors' impression that X-ray treatment was beneficial. (References.)

W. H. Crisp.

Belmonte González, Nicholas. **Retinal arteriovenous index.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 442-445.

The diameter of the retinal arteries and veins is very difficult to measure and the percentage of error is very great. The author recommends finding the relation of the diameter between arteries and veins by means of the enlargement of the fundus picture. This method permits the measurement of the vessels in tenths of millimeters. He found that normally the arteriovenous index is between 0.70 and 0.90. The application of this method is valuable for the early diagnosis and prognosis of hypertensive retinopathy. Several cases are reported with illustrations.

J. Wesley McKinney.

Belmonte Gonzáles, Nicolas. **A contribution to the study of experimental hypertensive retinopathy.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, March, pp. 213-220.

This experimental work was done on dogs, whose fundi were carefully observed. Fifteen to eighteen months before the observations, the dogs had hypertension with a range between 160 and 200 mm. Hg, whereas 120 mm. is normal. They did not show alteration in the urine nor elevation of the urea in the blood. The disturbances observed in the fundus consisted of tortuosity of the vessels, disturbances at the arteriovenous crossing, thickening of the arterial walls and rarely hemorrhages. In the dog, an experimental chronic nephrogenous arterial hypertension produces a fundus picture similar to that of essential hypertension in man. Complete renal insufficiency provoked by bilateral nephrectomy does not produce elevation of the blood pressure, and does not give any retinal disturbance. The tightening of both ureters produces in the fundus the alterations of function necessary to produce angiospastic retinitis. (Colored illustrations.)

J. Wesley McKinney.

Campos, R. **The respiration and glycolysis of the retina after section of the optic nerve.** Rassegna Ital. d'Ottal., 1947, v. 16, May-June, pp. 169-185.

The optic nerve of the rabbit was cut across within the orbit in a manner

which left the central retinal and long ciliary vessels intact. The respiration of the retina was then measured in Ringer's solution by the Wardburg method, direct and indirect. In the same way the aerobic and anaerobic glycolysis was measured at various periods of time after the section of the nerve. Tests demonstrated that the metabolism of the retina maintains its characteristics even five months after the nerve has been cut. At this time the ganglion cells are completely degenerated, as shown by the histological study of the retina. (2 figures.) Eugene M. Blake.

Cerboni, F. C., and Malamud, B. **Concerning three cases of asteroid bodies in the vitreous.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Aug., p. 213.

The authors present three cases of asteroid bodies in the vitreous. Two of the patients had normal vision and the other had senile lens opacities which lowered the visual acuity. There was no intraocular disease in any of the eyes. The condition is briefly discussed, with special emphasis on the differential diagnosis. (Illustrations, bibliography.) Plinio Montalván.

Dejean, C., and Laporte, P. **Some clinical manifestations of tuberculous macular retinitis.** Arch. d'Opht., 1946, v. 6, no. 4, pp. 397-412.

The authors describe four morphologic types of tuberculous involvement of the macula. The first type has been described under the name "solitary tubercle of the macula" and is characterized by cotton-wool exudates in the macular region. There is definite swelling associated with it. The condition persists for weeks and months and can develop into retinitis proliferans, or can become absorbed, leaving a large area of chorioretinal atrophy.

The second type, known as central serous retinitis, is characterized by an intense macular edema, leading to the formation of a hemispheric bulla or a sort of serous cyst. The retinal vessels undergo a sharp bend when they reach the edge of the bulla. The evolution of this condition is described as being sluggish, often prolonged over several years and leading finally to an atrophy of the macula. It is often accompanied by vague ocular, orbital, and periorbital pain, tearing, and sometimes mild hypertony.

A third clinical type, known as brown macular retinitis, is not well known but is nevertheless of relatively frequent occurrence. It was noted particularly in prisoners of war returning from Germany. It is characterized by a brick red or brownish coloration of the macular region with an irregular and roughened appearance but with conservation of the foveal reflex. There is sometimes an alveolar appearance surrounding the fovea. The condition is described as evolving in four successive stages: (1) the brick red plaque stage, (2) the roughened brown plaque stage, (3) the brown alveoli or nodule stage, and (4) the black pigmentation stage.

The fourth type, known as radiating retinitis, is characterized by numerous whitish lines which diverge from the macula like the rays of the sun. The authors conclude that the ophthalmoscopic picture of this type is diagnostic.

The report is terminated by a discussion of etiology and therapy in which the authors express their regret that they were unable to control their studies by anatomical, bacteriological, and serological tests. They believe that a significant response to tuberculin therapy in these cases is evidence in favor of a tuberculous etiology.

The article is beautifully illustrated with eight drawings in color.

Phillips Thygeson.

Gimenez Ruiz. **Retinitis proliferans and tuberculosis.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, March, pp. 226-233.

Two adult men had recurrent hemorrhages in the vitreous in the year before the examination. The fundus showed the classic picture of retinitis proliferans. The origin of the retinitis was said to be tuberculosis and in one of them Koch's bacillus was found in the sputum. J. Wesley McKinney.

Haridas, G. **Waren Tay-Sachs disease in a Chinese infant.** Brit. Jour. Ophth., 1947, v. 31, July, pp. 428-436.

This typical case of amaurotic family idiocy is presented because it is the first case of this disease ever observed in Malaya. Its occurrence in a non-Jew is of interest because it is widely believed that the disease is entirely racial. The infant, 13 months of age, was seen because of convulsions. Of his family history nothing could be learned since the parents never returned after the baby's admission. The child was blind, suffered progressive hydrocephalus, paralysis of all limbs and severe muscular wasting. Funduscopy revealed marked pallor of both discs and a purple-red macular spot on a milky white background in each eye. He died at the age of 20 months and 20 days of terminal lobar pneumonia. Autopsy report was not available.

Morris Kaplan.

Kettesy, A. **Technical improvements in the diathermy operation for detachment of the retina.** Brit. Jour. Ophth., 1947, v. 31, July, pp. 436-441.

The author expresses much dissatisfaction with the two types of coagulation treatment available. The perforating needle leaves the eye too soft and the sclera too wet for satisfactory technique and the Safar pins are awkward to hold in the forceps and are much too easily dislodged while further insertions are being made. He describes a new pin and forceps which has given him much satisfaction during the last three years. The pin is made of polished stainless steel with a round, flat head 0.3 mm. thick and 1.5 mm. in diameter. The length varies from 2 to 6 mm. It is cylindrical with a sharp conical point. The forceps is angular with grooves along three margins of the ends into which the pins fit securely. During the operation the pins are kept in flat cork plates. On a wood or plastic model of an eye made twice normal size, the procedures are sketched and planned carefully before each operation. The tear and the area of detachment are outlined. The longer pins, used for localization, are carefully watched with the ophthalmoscope and the shorter ones are used for the actual coagulation. (7 diagrams.) Morris Kaplan.

MacLean, A. L., and Brambel, C. E. **Dicumarol and rutin in retinal vascular disorders.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1093-1108. (1 table, 6 figures, 19 references.)

Magitot, A. **Clinical electrical retinography.** Ann. d'Ocul., 1947, v. 180, March, pp. 169-177.

The electroretinogram resembles the electrocardiogram in graphically electrically expressing organ function. The necessary apparatus consists of an illuminating and receiving-recording unit. The former includes an electric filament source, condensors, diaphragms, a rotary shutter, a tilted mirror, and a distance adjustment mechanism, all encased and suspended from a wall bracket. The recording unit consists of a contact glass electrode con-

nected by means of a head band, with a delicate galvanometer, and a recording drum.

The first phase in the electroretinogram is a slow component which corresponds with the initial current passage through the optic nerve. The second phase is more rapid and corresponds with rod and cone function. The third phase, like the first, is slow, and corresponds to the terminal current passage through the optic nerve. On the chart the first phase rises, the second is variable, and the third declines. The patient should remain in a dark room for thirty minutes before the E.R. is made. The lids are anethesized by the Van Lint method and kept open with a blepharostat. In 92 of the 102 patients examined an electroretinogram was obtained on the first trial. Interpretation was difficult in approximately 20. An illumination of 20 lux and a stimulation time of $\frac{1}{25}$ second were adopted. The electroretinograms were arbitrarily divided into four groups. In the first group all phases of the graph were diminished; among the conditions observed were retinal detachments, pigment degenerations, and glaucomas. In the second group, the negative phase dominated the graph. Circulatory disturbances were more frequent in this group. In the third group all three phases were absent because there was no retinal function. In the fourth group all phases were equally subnormal. In several cases, a parallelism existed between the changes of the electroretinogram and the evolution of the disease.

Chas. A. Bahn.

Palomar Palomar, A. **Anticoagulant medication (heparin, dicumarol) in the treatment of thrombosis of the retinal veins.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, March, pp. 247-264.

Heparin was administered in four cases of thrombosis of the retinal veins, of which two involved the central vein and two one of its branches. Heparin was given intravenously in doses of 100 to 300 milligrams daily for 17 days. Dicumarol in doses of 100 to 200 milligrams was used orally, daily for 15 days, in eight cases of thrombosis of the central retinal veins and six in a branch. Improvement, only functional and not anatomic in some, was noted in all, especially where the medication was begun early. These drugs are contraindicated in hypertension, blood dyscrasias and icterus.

J. Wesley McKinney.

Plam, Erik. **On the occurrence in the retina of conditions corresponding to the blood-brain barrier.** Acta Ophth., 1947, v. 25, pt. 1, pp. 29-35.

The findings in this laboratory study on seven rabits confirmed the generally known incapacity of the retina to take vital staining with intravenously injected dyes, and its similarity to the central nervous system in that respect. The walls of the retinal vessels do not take the dye, which is in accord with the current opinion that the barrier to the passage of the dye in the central nervous system is formed by the vascular endothelium. The fact that the choroid which supplies nutrition to the outer layers of the retina, was found stained, whereas the retinal layers themselves did not take the stain, seems to indicate that the obstacle to the penetration of the dye in the retina must also be situated elsewhere than in the vascular wall. Louis Daily, Jr.

Wadensten, Lars. **A case of bilateral non-attachment of the retina.** Acta Ophth., 1947, v. 25, pt. 1, pp. 61-71.

The patient, a seven-months-old in-

fant, one of premature biovum twins, was brought to the eye clinic with the history that she did not fix her gaze like her sister, and that the pupils shimmered gray. In each eye there was a white membrane with a suggestion of vessels pressed tightly against the posterior surface of the lens; the anterior chamber was shallow, and the iris and lens protruded. There was no pupillary reaction in the right eye, and it was enucleated. The detailed microscopic description shows a non-attachment of the retina, which was connected to the optic papilla by a cord of glial tissue. The literature contains about twenty reports of this congenital deformity, but only one case, that of Magnus, is analogous to the one here reported. The literature on the pathogenesis of this anomaly is reviewed. (3 photomicrographs.) Louis Daily, Jr.

Walbeek, K. **A case of degeneration of the macula lutea caused by central choroiditis.** Acta Ophth., 1947, v. 25, pt. 1, pp. 37-45.

A detailed clinical and histological description is given of an eye with a tumor-like mass in the macula which was enucleated because of hemorrhages and secondary glaucoma. The patient, a woman 40 years old, with a history of gall bladder disease, developed a central choroiditis in the left eye with vitreous opacities and involvement of the optic nerve. After five years she developed the tumor-like mass in the right eye, which was enucleated one year later. The histologic diagnosis was disciform macular degeneration. The literature on the etiology of this condition is reviewed, and it is argued that the history of a previous inflammatory process in the other eye supports the belief that the lesion is inflammatory, rather than vascular or degenerative in origin. The site of the inflammatory process is in the choriocapillaris. (5 illustrations.) Louis Daily, Jr.

11

OPTIC NERVE AND TOXIC AMBLYOPIAS

Caminero, G. M. **Investigations on the pathogenesis of quinine amblyopia.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 360-366.

Among the large number of malaria patients seen in North Africa in 1941 to 1943, Caminero found nine cases of quinine amblyopia. These patients were all seen early, and were all anemic people, with pale conjunctiva and dilated pupils. In addition to the usual symptoms, they had a diminished light sense, and delayed adaptation to light as well as darkness. They were followed for two years, and although they recovered their visual acuity, a constriction of the visual field remained. Caminero raises the question of a susceptibility to quinine amblyopia as a factor other than the toxicity of the drug itself. If such a factor exists, are there people sensitive to quinine, or does the malaria produce such a sensitization? Hemoglobinuric fever can be produced in malaria patients by the ingestion of very small quantities of quinine. Seeking to reveal the cause of this sensitization Caminero investigated the elimination of quinine in normal people and in malaria patients with and without quinine amblyopia. In normal individuals and in malaria patients quinine begins to be eliminated through the urine 25 minutes after ingestion, reaches the maximum after six hours, and is completely eliminated in three days. Of seven patients with quinine amblyopia the elimination was normal in three, somewhat delayed in two, and definitely delayed in two.

The total quantity of quinine eliminated was determined in only one case with amblyopia and found normal. Studies of kidney function failed to reveal any abnormalities. Ray K. Daily.

Kauntze, Ralph. **Subacute bacterial endocarditis with onset as optic neuritis.** Brit. Heart. J., 1947, v. 9, Jan., pp. 34-37.

Two cases of subacute bacterial endocarditis are presented in the first of which there was retrobulbar neuritis at the onset and in the second bilateral papilloedema. Irwin E. Gaynon.

Leinfelder, P. J., and Robbie, W. A. **Experimental studies in retrobulbar neuritis.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1135-1143. (8 tables, 16 references.)

Roussel, F., and Weekers, R. **Changes of the critical flicker frequency in tobacco intoxication.** Ophthalmologica, 1947, v. 113, April, pp. 215-223.

In a previous communication (Ophthalmologica, v. 112: 305, 1946) the authors described a method of measuring the critical flicker frequency of eccentric retinal areas and advocated the use of this method in the follow-up of diseases of the optic nerve. The paper under review deals specifically with cases of tobacco intoxication. The patients showed a lowering (slowing-down) of the critical flicker frequency in the region of the centrocecal scotoma, paralelling the latter in severity and extent. A slight lowering of the critical flicker frequency was found to persist after the visual field had returned to normal.

Peter C. Kronfeld.

Sanchez Mosquera, M. **Ocular cysticercus.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, March, pp. 234-246.

(See Section 17, Systemic diseases and parasites.)

12

VISUAL TRACTS AND CENTERS

Beck, D. J. K. **Upper parietal meningioma showing Foster-Kennedy syndrome.** Bristol Med. Chir. J., 1947, v. 64, Spring, pp. 11-12.

Whereas Kennedy stated that the syndrome associated with his name is a diagnostic criterion of the existence of an expanding lesion in the anterior fossa, this case illustrates the need to interpret the syndrome in the light of other signs and to pay attention to the stage at which the eye signs develop.

F. H. Haessler.

François, J. **Binasal hemianopsia.** Ophthalmologica, 1947, v. 113, June, pp. 321-343.

The author describes in detail two cases of neurinoma of the acoustic nerve and one case of opticochiasmatic arachnoiditis, all verified by operation and all showing chiefly binasal field defects. He compares the findings in his three cases with those in 49 similar surgically explored or pathologically examined cases from the literature. He also reviews the anatomy of the region of the chiasma. He concludes that the main mechanism concerned in the causation of binasal hemianopsia is a disturbance of the normal spatial relationship between the supero-temporal aspect of the optic nerves and the anterior cerebral arteries. The arteries may press against the nerves or the nerves may be crowded against the arteries. (11 figures.) Peter C. Kronfeld.

Nichelatti, Paolo. **Adie's syndrome in hysteric subject.** Boll. d'Ocul., 1946, v. 25, July-Sept., pp. 421-432.

A nun, 42 years of age, when in-

formed that her left pupil was larger than the right, complained of neuralgic pains of the left side of her face and photophobia, and her vision became reduced to 2/10 in each eye. Left pupillary reactions were as slow in normal daylight as in the dark. Her left pupil was enlarged when the patient was kept in a dark room for about an hour and became contracted when the patient was exposed to intense light for an hour. Consensual and accommodation reactions were also slow. The diagnosis was based on these changes of the left pupil, on the lack of deep reflexes, and the negative serologic examinations. The other ocular disturbances were hysteric in nature and disappeared under appropriate treatment. (Bibliography.) Melchiore Lombardo.

13
EYEBALL AND ORBIT

Casanovas, José. **Orbital osteomas.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 335-347.

A review of the literature, and brief reports of six cases are presented. Two patients had growths in a sinus, two of the tumors arose from the orbital walls with a broad base, and two tumors were pedunculated. In one case osteoma was bilateral. In two patients the exophthalmos almost caused ocular dislocation. Five cases were dealt with surgically. Histologic examination showed that two of the tumors consisted of compact bone, and three were spongy. (8 illustrations.)

Ray K. Daily.

Shannon, C. E. G. **The exophthalmos of hyperthyroidism.** Pennsylvania M.J., 1947, v. 50, August, pp. 1155-1159.

The author reviews briefly the current view of the relationship of exophthalmos to hyperthyroidism and reports five illustrative case records.

F. H. Haessler.

14
EYELIDS AND LACRIMAL APPARATUS

Busacca, A. **A simple and easy method of blepharoplasty.** Ann d'Ocul., 1947, v. 180, May, pp. 288-292.

Disinsertion of the external palpebral ligament facilitates marked displacement of the upper and lower lids. Greater advancement of the skin to cover traumatic or other colobomas is thus possible. Following local anesthesia and the administration of coagulin, venine, or other coagulating agents, external canthotomy to the orbital rim is performed. A subcutaneous vertical incision about one-fourth inch in the external palpebral ligament is made. The coloboma is freed of cicatricial tissue. A cutaneous incision is made roughly parallel to the upper or lower lid border and extending from the coloboma margin almost to the orbital rim. The skin is undermined to form a flap. The edges of the coloboma are approximated by a mattress suture horizontally placed, and the lid flap is drawn over the coloboma laterally and sutured. The canthotomy wound edges are approximated by laterally advancing, with a suture, the skin of the upper or lower lid approximately one-half inch. (11 figures.) Chas. A. Bahn.

Dollfus, M. A. **The irradiation treatment of the lid epitheliomas.** Report presented at the meeting of the Société d'Ophthalmologie de Paris, 1946, Nov., 160 pp.

The extensive research work on the irradiation treatment of lid epitheliomas carried on by the author and his collaborators at the Foundation Curie from 1927 to 1940 is reported.

The first part deals with the history, pathology and clinical manifestations of lid epithelioma, and the differential diagnosis from chronic ulcerative blepharitis, tuberculous and syphilitic lesions, and nevocarcinoma, is described.

The second part—the physical properties of radio-active substances in general, the characteristics of the different rays, and the occurrence and potential dangers of secondary radiation are discussed. The units of radium element and radium emanation, the Curie, are described in detail.

Other points of importance in the specification of every radium application are the shape and size of the carriers, their number, the kind and density of the primary and secondary filters, the positions and the distance between carriers and irradiated tissue, the strength of the carrier, the time of irradiation in hours, the energy as expressed in the units described, and the surface and depth extension of the irradiated tissue. A plastic material of beeswax 100 gm., paraffin 100 gm., and fine sawdust 25 mg. is molded on the face in varying thickness depending on the distance required for the irradiation. Radium needles in four different strengths and lengths, tubes, and gold seeds containing 1 to 2 millicuri radon are used for the contact treatment. A mixed irradiation treatment, namely surface irradiation plus curiepuncture, was used in infiltrating cancers.

The third part deals with X-ray treatment. The origin and peculiarities of X rays, the importance of the different filters, the irradiation with single large or divided small doses, and the results and dangers of this treatment are described in detail. The doses for circumscribed lesions vary from 2000 to 5000 r, most frequently 2600 to 3600 r. For extensive lesions 5000 r were given. The maximal doses were 9600 r. The exact dosage is important because of the dangers of an insufficient treatment which not only might cause a radio resistance, but might also change the clinical form of the epithelioma to a more malignant type.

The contact-therapy of Chaoul, a comparatively new method in the irradiation of lid epithelioma is discussed. The principle of this method is the surface utilization of rays which penetrate but little and rapidly decrease in effect in the sub-epithelial layers. Their range is only two centimeters of surface diameter and one of depth range, which limits their general use but coincides with the average size of lid epithelioma.

Part four summarizes the pre-radiation care and immediate effects of the irradiation on the epithelioma. Part five contains the reports of the results and the failures of those treatments. The potential danger of ocular complication makes necessary a close collaboration of radiologists and ophthalmologists during every stage of the irradiation. The after care is especially important as patients with lid epithelioma have to continue in constant supervision for at least three years. Recurrences usually appear during this time.

In part six the author discusses the ocular complications and the means to avoid them. The improved methods, as well as the use of metal, especially lead shells in the form of a prothesis over the eyeball, have reduced the frequency of complications, but the latter can never be completely avoided. Early complications are mostly benign, late complications mostly insidious and of uncertain prognosis. Common complications are hyposecretion of the lacrimal glands, interstitial keratitis, corneal necrosis, iridocyclitis, secondary glaucoma, and opacities of the lens.

Young lenses are especially vulnerable. Degenerations of the retinal and choroideal vessels as sequelae of irradiations are rare.

In part seven the results of irradiation treatment are compared with the results of diathermy and surgical treatment. This comparison is not complete because of the lack of adequate reports concerning the late results of surgical treatment. A table shows the results of radium and X-ray treatment during the last 25 years. (379 references, 5 tables.) Alice R. Deutsch.

Fine, M., and Waring, W. S. **Mycotic obstruction of the nasolacrimal duct (candida albicans).** Arch. of Ophth., 1947, v. 38, July, pp. 39-42.

Numerous reports may be found in the literature of obstruction of the lacrimal passages produced by various fungi. Streptothrix and leptothrix are mentioned in most textbooks as the organism commonly encountered. Reports of mycotic obstruction of the nasolacrimal duct, however, are notably lacking. In this paper two cases of mycotic obstruction of the nasolacrimal duct are described, with identification of the yeast as C. albicans in one case. Recovery was spontaneous and immediate following extrusion of the castlike obstruction of the duct. (12 references.) R. W. Danielson.

Godtfredsen, Erik. **Relation between Sjögren's disease, the Plummer-Vinson syndrome, and ariboflavinosis.** Acta Ophth., 1947, v. 25, pt. 1, pp. 95-109.

The literature on the three syndromes is reviewed, and their interrelation analyzed in the hope of throwing some light on the etiology and pathogenesis of Sjögren's syndrome. In addition a report is made of an analysis of 23 cases of Sjögren's syndrome collected since 1943 from the Ophthalmic Departments of the County Hospital, Gentpfte, The Finsen Institute, and the State Hospital in Copenhagen. The patients were all women in the postmenopausal period. Twenty patients had chronic progressive polyarthritis. The articular affection had persisted from 1 to 30 years before the affliction was recognized as Sjögren's syndrome. The Plummer-Vinson syndrome, the most characteristic features of which are epithelial lesions in the upper alimentary tract and sideropenia, formed a part of the pathologic picture in three patients. All had greatly reduced or completely abolished lacrimal secretion, and most of them were treated for about five years with irritative instillations before the diagnosis of keratoconjunctivitis sicca was made. None had the superficial vascularization characteristic of ariboflavinosis. Treatment with viatmine B and iron relieved the alimentary tract symptoms in the three patients with Plummer-Vinson syndrome but in the others it was entirely ineffective. Sideropenia or riboflavin deficiency appear to have no etiologic significance in Sjögren's diseases, and in spite of the numerous common clinical features, it is concluded that Sjögren's disease differs essentially from ariboflavinosis and the Plummer-Vinson syndrome. Louis Daily, Jr.

Redslob, E. **Palpebral entropion from malformation of the Meibomian glands.** Ann. d'Ocul., 1947, v. 180, May, pp. 263-266.

An infant, seven months of age, was operated upon because of entropion and trichiasis. Under local anesthesia the tarsus was removed. Microscopically, a small circumscribed inflammatory zone and two malformed rows of Meibomian glands, traversed by new

formed blood vessels were observed. In the embryo the two lids are held together by an epithelial bridge at about the time the Meibomian glands are formed. The malformation apparently occurred at this time. Among the diagnostic conditions differentiated are fatty and amyloid degeneration, gumma, and obliterative endarteritis.

Chas A. Bahn.

Schuessler, W. W., and Filmer, G. A. **A method for restoration of the cilia of the eyelids.** Plastic and Reconstructive Surg., 1947, v. 2, July, pp. 345-347.

The authors present a method of restoring the cilia to the eyelids with a vertical hair-bearing graft removed from the eyebrow. This is in contradistinction to the usual method which utilizes a horizontal section. For defects longer than the vertical dimension of the eyebrow, two sections can be removed.

The excellently reproduced photographs that accompany the one case report illustrate the more normal spacing and direction of the cilia which can be obtained. Alston Callahan.

15

TUMORS

Casanovas, Jose. **Orbital osteomas.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 335-347. (See Section 13, Eyeball and orbit.)

Höhr Castán, Jose. **Ocular xeroderma pigmentosum.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 487-491.

A boy, 10 years of age, had a small whitish tumor mass, a xeroderma pigmentosum, on the lumbus of the left cornea for one and a half years. The patient also had several plaques of xeroderma pigmentosum in the cervical and sternal zones. All other examinations were negative.

J. Wesley McKinney.

Huggert, A., and Hultquist, G. T. **True glioma of the retina.** Ophthalmologica, 1947, v. 113, April, pp. 193-202.

Only two cases of true retinal glioma consisting almost exclusively of adult glial cells have been reported, one by Dejean and one by McLean (Arch. of Ophth. 18:255). One new case is put on record in the paper under review. A male patient, age 77 years, presented himself at the eye clinic of the Caroline Hospital, Stockholm, with the complaint of gradual deterioration of the vision of the left eye for several years and pain and inflammation for the last two weeks. The eye was found to be in a state of absolute glaucoma. A yellowish mass, resembling a hypernephroma, filled the entire anterior chamber. During the enucleation the conjunctiva and Tenon's capsule were found to be indurated and difficult to detach. Hard yellowish masses occupied the inferior and nasal portions of the orbit. In places these masses had disintegrated into curd-like material. A tumor mass filled the interior of the globe almost completely; it had destroyed or replaced the retina and had invaded the optic nerve. The choroid was torn in several places but not thickened, the sclera appeared uninvolved.

Histologic examination showed that the tumor consisted chiefly of polymorphous cells with honeycombed, vacuolated cytoplasm. Silver impregnation revealed numerous argentophilic cells with a few short, scantily branched processes. In most places, the tumor was compact in structure with sparse bands of connective tissue between the cell masses. Pseudo-rosettes around blood vessels could be seen in moder-

ate numbers. The description is not clear with regard to the amount of necrosis, but its presence in the center of groups of tumor cells is mentioned. There was an abundance of mitotic figures and, as mentioned before, definite polymorphism of the nuclei. The authors classify the tumor as a true retinal glioma of the oligodendroglioma type. The extraocular masses are thought to be metastases. No statement is made about the postoperative course and termination of the disease.

Peter C. Kronfeld.

Hughes, L. W., and Ambrose, A. **Massive melanosarcoma of the eye.** Arch. of Ophth., 1947, v. 38, July, pp. 111-112.

This case is recorded not so much for its pathologic interest, because the tumor is one of the common ones affecting the eye, but because of its spectacular size. A photograph of this far advanced tumor is given. Paradoxically, two years after evisceration of the orbit the patient shows no recurrence.

R. W. Danielson.

Garcia Miranda A. **Fibroma of the orbit.** Ophthalmologica, 1947, v. 113, March, pp. 149-156.

A white male, 25 years of age, complained of slowly increasing protrusion of his left eye of about seven years' duration. Examination revealed a palpable hard tumor in the upper temporal portion of the left orbit. Roentgenologic findings were normal. The tumor was removed by the Kroenlein technique. It was well circumscribed and located outside the muscle cone. Its place of origin could not be ascertained. The histologic examination revealed a fibroblastic tumor consisting mainly of spindle-shaped cells in a criss-cross but not truly fascicular arrangement. There was an abundance of heavy collagenous and of finer reticulin-like fibers. The author considers the tumor to be benign and of mesodermal origin, but is not entirely certain of his diagnosis because of the abundance of cellular elements. The main features of the tumor are shown in three good photomicrographs. There apparently was no opportunity for postoperative follow-up.

Peter C. Kronfeld.

Pfeiffer, R. L. **Tumors of the eye and orbit.** N.Y. Acad. Med. Bull., 1947, v. 23, July, pp. 410-419.

The author describes the clinical manifestations of naevus, precancerous melanosis, malignant melanoma, retinoblastoma, lymphatoid disease involving the eye, granuloma, neurofibromatosis, cholesteatoma, and adrenal neuroblastoma.

Irwin E. Gaynon.

16

INJURIES

Adler, F. H., Fry, W. E., and Leopold, I. H. **Pathologic study of ocular lesions due to lewisite (β-chlorovinyldichloroarsine).** Arch. of Ophth., 1947, v. 38, July, pp. 89-108.

The pathologic changes in the rabbit eye injured by lewisite are described. In the early stages changes appeared in the stroma which may be interpreted as a rapidly progressing necrosis of the whole stromal layer. This was seen in the loss of the nuclei of the corneal fibers, the loss of staining ability of these fibers and their loss of outline. These changes were first seen at the end of six hours and reached the maximum in 24 hours. The infiltration of the stroma began at the periphery at the 24-hour stage and was of poly-

morphonuclear cell type. This infiltrate was replaced by a round cell infiltrate at the end of the 10-day stage. Vascularization did not make its appearance until the end of five days. This vascularization involved all layers of the stroma but was most prominent in the middle layers. In 14 days the vascularization was fairly intense. In any eye treated with BAL there were no changes that could be attributed specifically to the treatment. The changes were similar to those observed in the untreated eye but were of milder degree. (15 figures.)

R. W. Danielson.

Atkinson, W. S. **Exact surface localization of ophthalmoscopically visible foreign bodies in the vitreous chamber.** Arch. of Ophth., 1947, v. 38, July, p. 110.

Small foreign bodies in the vitreous chamber which are entangled in the retina and choroid or embedded in the sclera are often not pulled loose with the magnet unless it is applied close to or directly over the foreign body. In order to make the incision exactly at the point where the foreign body can be seen, a Walker retinal detachment pin is first inserted as a pilot as close to the area as possible. The incision is then adjusted according to the relative positions of the foreign body and the pin.

R. W. Danielson.

Marin Amat, M. **A case of a foreign body imbedded in the external layers of the sclera.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, April, pp. 375-379.

Marin Amat reports an industrial injury, in a man 26 years old, whose right eye was perforated through the cornea by a foreign body, which was found by X-ray examination. Misleading yellowish conglomerations were present in the lens, and on the retina. Attempts at extraction were unsuccessful, and the eyeball, greatly traumatized by these procedures, was finally enucleated. Histologic examination showed a fusiform, irregular, sharp piece of iron encysted in the outer layers of the sclera.

Ray K. Daily.

Rones, B., and Wilder, H. C. **Nonperforating ocular injuries in soldiers.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1143-1160. (25 figures, 3 tables.)

Savin, L. H. **The effect of aluminium and its alloys on the eye: a report presented to the vision committee of the medical research council.** Brit. Jour. Ophth., 1947, v. 31, Aug., pp. 449-502.

This comprehensive study is based on two clinical observations and extensive experimental work.

The author reviews the literature and presents two cases of intraocular aluminium foreign bodies. In each instance the fragment became coated and left multiple imprints due to shifting position before disintegrating into white powder after many months. Good vision was retained in one case.

For experimental study 34 intraocular implants were made. It was found that the ocular reaction was more severe with higher amounts, but there was no clinical difference between pure aluminium and various alloys. Both groups showed lens opacities, mild inflammatory changes in the iris, atrophy of the iris, retinitis proliferans and vascularization of various parts of the eye. Aluminium causes more destruction in the vitreous than in the anterior chamber. Early changes, chiefly vascular, occurred in tissues adjacent to the foreign bodies.

Fundus lesions showing widespread distribution of the aluminium in the tissues were present in nearly every case, no matter what the size or position of the implant. In six eyes there was apparently complete dissolution of the aluminium, but the author was unable regularly to obtain specific stains of the section to be sure of the true distribution in the ocular tissues.

Also noted in the experimental animals were bullous keratitis, staphyloma, zonular keratitis, interstitial and deep keratitis, pigmented cornea and folds in Descemet's membrane.

Aluminium had previously been regarded as comparatively inert in the eye. The author has conclusively shown that it causes widespread low-grade inflammatory and degenerative changes, seen histologically as well as clinically. Although aluminium and its alloys are not so destructive as iron and steel, these intraocular foreign bodies call for operative removal.

There is a graphic summary in which the findings in the eyes of the animals are made perspicuous by diagrammatic drawings. (21 figures of which 9 are in color.) O. H. Ellis.

Sorsby, A., Haythorne, J., and Reed, H. **Further experience with amniotic membrane grafts in caustic burns of the eye.** Brit. Jour. Ophth., 1947, v. 31, July, pp. 409-418.

This is a report of additional experience of the use of human amniotic membrane in chemical burns of the eye. In these severe burns, the eyes were generally found to be nearly white in 3 to 5 days after grafting and they were usually normal by the end of the week. Now 28 additional cases are reported, 21 of burns by lime, 5 by sodium hydroxide and 2 by fireworks. Corneas were involved in all, and yet in only three eyes was the vision unsatisfactory. Terminal clarity of corneas was directly related to the interval between injury and treatment. The amniotic membrane is apparently tissue specific in its action. It does not lead to clarification of severe corneal damage but it does prevent corneal damage caused by a persistent raw conjunctiva. The details of preparing the amnion for grafting are described. Morris Kaplan.

Tanzariello, R. **The tolerance of the eye to aluminum and its alloys.** Rassegna Ital. d'Ottal., 1947, v. 16, May-June, pp. 199-223.

Small pieces of aluminum and of various commercial compounds containing aluminum were introduced into the vitreous chamber of rabbits' eyes. The foreign bodies were retained from 10 to 187 days and the eyes were observed frequently with the ophthalmoscope. One of the compounds contained 90 percent of copper and this was as poorly tolerated as pure copper. Other compounds, with only 3.5 percent copper were much better tolerated. Pure aluminum caused practically no reaction. The author concludes that when intraocular foreign bodies of alloys of aluminum enter the eye, those which contain copper demand early efforts at removal, whereas pure aluminum may safely be followed for long periods. (74 references.) Eugene M. Blake.

17

SYSTEMIC DISEASES AND PARASITES

Casari, G. F. **Ocular manifestations of erythema nodosa.** Rassegna Ital. d'Otta[l] 1947, v. 16, May-June, pp. 228-250.

The ocular manifestations of erythe-

ma nodosa are analogous to the lesions elsewhere. The picture is that of an allergic reaction, which may be homoallergic, heteroallergic or para-allergic. The last named seems the most satisfactory explanation. Some cases are especially difficult to classify. The eye manifestations are particularly important because they may be isolated instances of the disease or may precede the manifestation in the skin and mucous membranes. Three cases are reported in which ocular lesions that had the appearance of phlyctenules complicated the general eruption. The literature is reviewed and a bibliography appended. E. M. Blake.

Cordello, G. **Ocular symptoms in subarachnoid hemorrhage.** Rassegna Ital. d'Ottal., 1947, v. 16, Jan.-Feb., pp. 50-63.

Subarachnoid hemorrhage may be a result of a general disease, such as infection, liver damage, blood disease or an intoxication. The source of the bleeding is either a ruptured aneurysm (frequently the result of congenitally defective structure of the vessel) or functional vasoneurotic disturbance, often endocrine in origin.

The ocular manifestations are disturbances of the motor nerves, changes in the optic nerves, particularly edema, retinal hemorrhages, and a group of symptoms, such as nystagmus, verbal blindness, violent retrobulbar pain, and loss of sight.

Three cases are reported in detail.

Eugene M. Blake.

Dekking, H. M. **Tropical nutritional amblyopia ("camp eyes").** Ophthalmologica, 1947, v. 113, Feb., pp. 65-92.

"Nature, that most unscruplous vivisectionist, has just finished one of her greatest experiments, a war. Of all her vast laboratories, the South East Asia theater of war has yielded some very remarkable results from an ophthalmologic standpoint. Hundreds of thousands of men, women and children have been kept in cages for almost four years, and have been subjected to all kinds of deficient diets and to incredible physical and mental strains." Under these circumstances, which the author has well described and hardly exaggerated, a tropical nutritional amblyopia (called "camp eyes" by the Dutch physicians) has occurred on a much more extensive scale than ever before. Striking features of the disease are its occurrence in the concentration camps of South East Asia and not of Germany and its predilection for adult males of light complexion. Among women the disease is so rare that "in many women's camps not even the name (of the disease) was known." The onset is usually gradual, with bilateral irregular paracentral scotomas, nyctalopia and a tingling or burning sensation in the feet and legs. The author has not seen the earliest stages, but other physicians have reported congestion of the retinal vessels and small retinal hemorrhages in some of the patients (percentage not known). In the late stages the maculae may be slightly abnormal and the temporal halves of the discs are pale. The prognosis is bad. Adequate food plus supportive measures continued for periods of eight months and longer have not brought about any improvement.

While in the concentration camps the patients' food consisted of red or white rice and a very diluted vegetable soup. Thus, there existed a deficiency of all vitamins as well as of animal proteins and of fat. The author discusses all likely causes of the amblyopia and ar-

rives at the conclusion that the disease "cannot be ascribed to one single agent, but that it is most probably due to gross deficiency of B vitamins, plus an intoxication (tobacco?), plus, perhaps the intense tropical sunlight as an aggravating factor." Peter C. Kronfeld.

Grant, W. T. **Complete removal of craniopharyngioma with recovery from blindness.** Bull. Los Angeles Neurol. Soc., 1947, v. 12, March, pp. 53-58.

A two-year-old Mexican boy had complete blindness for three weeks which began 12 days after a head injury. The optic discs were normal. The left pupil responded to light two days after the extirpation of a craniopharyngioma and the child was able to see on the seventh day. Irwin E. Gaynon.

Rugg-Gunn, A. **A case of recurrent apthous uveitis with associated ulcus vulvae actum. (Lipschütz).** Brit. Jour. Ophth., 1947, v. 31, July, pp. 396-409.

Aphthous uveitis is a new and rather rare clinical entity which presents three main groups of symptoms. These are a periodically recurring uveitis, skin eruptions which consist of macular pustules that resemble those of secondary lues and recurrent erythema nodosum, and aphthus ulcers in the mouth and genitals. The eye symptoms appear late, though once established, progress rapidly toward deterioration and blindness. The etiology is unknown and it is particularly characterized by its resistance to any known treatment.

The author reports his observations of a woman, 22 years of age, who had recurrent uveitus, in alternating eyes, for over a year before other signs developed. Although she was resistent to several regimens of therapy she reacted best to intravenous protein. During the year it was felt that the infection was tuberculous. Buccal aphthae then appeared, followed by a severe aphthous ulcer of the vulva. The left eye progressed to blindness whereas the aphthous lesions apparently healed spontaneously during the latter months of a normal pregnancy. The skin lesions did not appear at all. The author insists that all signs point to a virus as the causative agent. (5 diagrams.)

Morris Kaplan.

Sanchez Mosquera, M. **Ocular cysticercus.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, March, pp. 234-246.

A man, 40 years of age, had noted defective vision in his right eye for three weeks. There was a gray haze, aching, and a burning sensation of the eye. Ophthalmoscopic examination showed a brilliant gray-blue perfectly spherical cyst in the optic nerve head which contained a tapeworm scolex complete with hooks and four suction discs. The cysticercus moved about constantly. Tenia saginata was also found in the feces. The cysticercus was removed after some attempts to kill it by means of radium applications and sulfanilamides. (Photographs.)

J. Wesley McKinney.

Schmidt, A. E., and von Albertini, A. **The ocular vessels in endangiitis obliterans (von Winiwarter-Buerger).** Ophthalmologica, 1947, v. 113, March, pp. 129:148.

Marchesani was the first ophthalmologist (1932) who considered endangiitis obliterans as the cause of vascular ocular diseases such as retinal periphlebitis, recurrent viterous hemorrhages with the associated uveitis, retinal vascular spasms, embolisms, and thromboses. Marchesani's view did not

become generally accepted. A. E. Schmid, one of the authors of the paper under review, in a previous publication (Ophthalmologica, 110:259, 1945) denied any relationship between endangiitis obliterans and retinal periphlebitis. The present study deals with the part played by Buerger's disease in spastic and occlusive diseases of the retinal vessels.

The pathology of the endangiitis process is described and illustrated. The earliest change is a transient fibrinous inflammation of the intima, followed by a chronic stage in which the arterial or arteriolar wall undergoes sickle-shaped thickening due to deposition of "fibrinoid" masses which gradually increase in thickness through additional fibrinoid deposition but also through organization and, later on, lipoid infiltration. The latter, however, is always a secondary process in contradistinction to the primary degenerative arteriosclerosis which is not a lumen-reducing disease. The preferred sites of endangiitis obliterans are the vessels of the lower extremities, the coronary arteries, the aorta and the cerebral arteries. The angiitic disease may cause secondary arterial occlusion distal to the specific lesion or secondary ("additional") thrombosis next to it; it may also be responsible for spastic aggravation of the existing vascular disease.

The findings in a number of cases studied pathologically by the authors supported by a critical survey of the literature leads them to the conclusion that ocular involvement is very rare in endangiitis obliterans. If ocular involvement does occur, it is secondary to localization of the disease in the carotid artery or its branches. In most of these cases the ocular involvement has been in the form of conjugate deviation, hemianopic scotomas, transient visual disturbances, transient diplopia, cortical blindness or papilledema. True intraocular vascular disturbances, such as arterial spasm, embolism or thromboses, have been extremely rare. In all these eye manifestations the primary site of the disease is in the carotid or its branches. Retinal hemorrhages may occur, but can always be distinguished from those of retinal periphlebitis which, the authors maintain, is unrelated to endangiitis obliterans.

Peter C. Kronfeld.

Shannon, C. E. G. **The exophthalmos of hyperthyroidism.** Pennsylvania M.J. 1947, v. 50, August, pp. 1155-1160.

The author reviews briefly the current view on the relationship of exophthalmos to hyperthyroidism and reports five illustrative case records.

F. H. Haessler.

Simonelli, Mario. **Focal infection in ophthalmology.** Riv. di. Oftalm., 1946, v. 1, Nov.-Dec., pp. 706-739.

The author reviews almost 200 papers and adds two observations. One patient had serofibrinous metastatic iridocyclitis after infection from a subcutaneous foreign body, the other an optic neuritis believed to be secondary to a periapical abscess. The latter recurred after eleven years.

K. W. Ascher.

Zewi, M. **Reiter's disease.** Acta Ophth., 1947, pt. 1, pp. 47-60. (See Section 5, conjunctiva.)

18

HYGIENE, SOCIOLOGY, EDUCATION AND HISTORY

Duke-Elder, Stewart. **Ophthalmology during the war and in the future.**

Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1073-1080.

Grant, W. M. **Students' model for slit lamp biomicroscopy of the aqueous humor.** Arch. of Ophth., 1947, v. 38, July, p. 109.

For familiarizing students with the biomicroscopic appearance of the normal and the abnormal aqueous humor a series of model eyes is of considerable value. The type of model which the author has found satisfactory in postgraduate teaching has a convex glass "cornea," a rubber "iris" and a glass "lens," with an "anterior chamber" which can be filled with various artificial "aqueous humors." The construction is described.

The following aqueous preparations have been found satisfactory. Distilled water simulates normal aqueous in that it gives the appearance of an "optically empty" anterior chamber. Diluted plasma with protein concentrations of 0.2 and 2 percent presents different intensities of the Tyndall effect. A dilute suspension of red blood cells in isotonic solution of sodium chloride, a suspension of cholesterol crystals, and a suspension of diatomaceous earth show the thermal convection currents.

R. W. Danielson.

Samuels, Bernard. **New York as an ophthalmological center.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1081-1093. (16 figures.)

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
904 Carew Tower, Cincinnati 2

News items should reach the editor by the 12th of the month

Deaths

Dr. Howell Llewellyn Begle, Detroit, Michigan, died June 5, 1947, aged 70 years.

Dr. Andrew Johnson Browning, Portland, Oregon, died May 20, 1947, aged 66 years.

Dr. Louis Richard Haas, Pittsburg, Kansas, died June 30, 1947, aged 44 years.

Miscellaneous

Gives ophthalmic books

Dr. Frederick W. Adams, formerly of Seattle, Washington, and now of Carmel, California, has presented his collection of books on ophthalmology to the new medical school of the University of Washington. The bound volumes number 215, and there are many unbound journals. Since his retirement, Dr. Adams has been a frequent exhibitor in the Physicians Art Association.

Rare Glasgow journal for sale

A copy of the *Glasgow Medical Journal,* dated 1829, bound in cloth and leather, is available for purchase. This is an historical item of great rarity and of great interest to ophthalmologists because it contains three classical articles by the pioneer eye surgeon, William Mackenzie, one time lecturer on the eye in Glasgow University. The price has been set at $50.00. Anyone interested may communicate with the Ophthalmic Publishing Company, 700 North Michigan Avenue, Chicago 11, Illinois.

Better Vision Institute meets

The Better Vision Institute held its third quarterly meeting in New York City on October 3rd. M. J. Julian, president of the Institute, gave a visual presentation and detailed descriptions of recent, current, and future projects.

Of immediate interest to professional members was the new series of 24 scientific leaflets just off the press. These leaflets are rich in information on practically all aspects of vision. For example, the leaflet entitled *Eyes on the Jump* deals with the process of reading and the value of professional guidance in improving reading habits. *Fit for Your Eyes* highlights the important duties of the ophthalmic dispenser and explains how his precise art can supply each individual with the glasses which will most help his appearance as well as his vision. *Learning to See* discusses the development of "seeing gaits" in people, and how good or bad ones may be acquired just as different walking gaits are acquired. *Thank you B. F.* is the scientific story of Franklin's contribution to human progress in the invention of bifocal lenses.

Other subjects covered in these leaflets range from the new telescope on Mount Palomar to heredity as it applies to eyes. But all topics are treated in a scientific manner, and the need for regular professional eye-care is consistently emphasized. The series of leaflets will be distributed to Institute members, and through them to schools, museums, and other educational centers.

Mr. Julian gave an outline presentation of the new set of educational charts which are being developed. These will comprise pictorial lessons on the human eye and how it sees, light and its relation to vision, color and color perception, lenses and how they bend light, faults of seeing, eye tests, and seeing skills. The charts will conclude with an "Eye-Q" quiz on a wide variety of visual themes.

Plans were also sketched for the Institute's general educational work during 1948. The meeting's guest speaker was Dr. Jules Backman, associate professor of economics at New York University.

New brochure ready

The Bausch & Lomb Industrial Vision Department announces that a new brochure for the ophthalmic profession is now available. Entitled *Ortho-Rater Scores and Clinical Examinations,* the booklet, Bulletin A-608, is designed to fill a need for correlating the Ortho-Rater scores with the clinical approach.

This timely brochure, produced in answer to professional requests for an explanation of the Ortho-Rater-clinical relationship, was held until comprehensive studies on the subject had been developed.

Requests for Bulletin A-608 may be made by letter or post card to the Industrial Vision Department, Bausch & Lomb Optical Co., Rochester, New York.

Societies

Reading has 69th meeting

The 69th meeting of the Reading Eye, Ear, Nose, and Throat Society was addressed by Dr. Gabriel Farrell, director of Perkins Institute and Massachusetts School for the Blind, Watertown, Massachusetts. The subject of his talk was "Modern Trends in Education of the Blind."

Brooklyn meeting

The Brooklyn Ophthalmological Society held its 101st regular meeting on October 23rd. The scientific program included a paper by Dr. Algernon B. Reese on "Discussion of Some Controversial Aspects of Ocular Tumors," and one by Dr. Alson E. Braley on "Virus Diseases of the Cornea." Dr. Mortimer A. Lasky presented a case report on "Progressive Essential Atrophy of the Iris." Dr. Leonard Posner was elected to membership.

Milwaukee society program

Dr. John G. Bellows, Chicago, was a guest speaker at the October 28th meeting of the Milwaukee Oto-Ophthalmic Society. His subject was "Use of Antibiotics in Ophthalmology: With Special Reference to Streptomycin." Dr. Emil Rothstein spoke on "Streptomycin in Otolaryngology."

New society organized

The newly organized Los Angeles Ophthalmological Society has elected the following officers: Dr. Orwyn Ellis, chairman, and Dr. John A. Bullis, secretary. The society meets at 6:30 P.M. on the third Tuesday of each month from September through June. The meeting place is at 3550 Wilshire Boulevard.

Announcements

Reservations for Havana meeting

All those who are planning to attend the III Pan-American Congress of Ophthalmology in Havana, Cuba, January 4 to 10, 1948, *and have not already done so,* should send their inscription fee of ten dollars together with a deposit for a room (ten dollars) to Dr. Miguel A. Branly, Edificio Bacardi 70, Piso, Havana, Cuba, at the earliest possible moment. Those who have confirmed reservations in the hotels will have no need to fear that their reservations will be cancelled.

Schoenberg Memorial Lecture

The first annual Mark J. Schoenberg Memorial Lecture will be held at the New York Academy of Medicine at 8 p.m., December 1st, under the joint sponsorship of the New York Society for Clinical Ophthalmology and the National Society for the Prevention of Blindness. The speaker of the evening will be Dr. Peter C. Kronfeld, of Chicago, head of the Illinois Eye and Ear Infirmary, whose subject will be "The Canal of Schlemm."

This lectureship was established as a memorial to Dr. Schoenberg's interest and original work in the control of glaucoma.

Personals

Good-will lecture tour

Dr. Daniel B. Kirby, New York, returned recently form a good-will lecture and conference tour of South America. Under the auspices of the Pan-American Association of Ophthalmology, Dr. Kirby visited Rio de Janeiro and São Paulo, Brazil; Montevideo, Uruguay; Buenos Aires, Rosario, and Cordoba, Argentina; Santiago, Chile; and Lima, Peru. Dr. Kirby reports that the South American oculists are very cordial and that many of them plan to attend the III Pan-American Congress in Havana and to visit the United States either before or after the Congress.

Addresses Oklahoma meeting

Dr. C. Wilbur Rucker of the Mayo Clinic, Rochester, Minnesota, was a guest speaker at the 17th annual meeting of the Oklahoma City Clinical Society, October 27th to 30th.

Guest speaker at Utah

Dr. A. Ray Irvine of Los Angeles spoke at the 52nd meeting of the Utah State Medical Association at Salt Lake City.